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MEDICINE IN THE NATIONAL DEFENSE PROGRAM

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THE fundamental objectives of Medicine in the National Defense Program may be stated as resting in three categories, namely, the provision of medical service to the armed forces, the provision of medical service to industry and the provision of medical service to the civilian population.

Provision of Service to the Armed Forces

The personnel of the Regular Army of the United States during peace has been so limited as to present no problem in securing adequate medical service. With the advent of war volunteers from the civilian profession have supplied the additional medical service required. In the Revolutionary War 1,400 medical men volunteered for service. The profession responded again in 1812. In the Civil War there were 12,000 with the Northern Army and it is estimated that 9,000 served with the Southern forces. In 1917 the personnel of the Regular Army Medical Corps numbered between six and seven hundred. At the time of the Armistice there were in uniform 31,000 medical officers, 5,000 dental officers, 2,000 veterinary officers, and in the Sanitary Corps a large number of specialists and administrators were required to round out the medical service of a large army. There were 20,000 nurses in the Army, 10,000 of whom served overseas, while the enlisted men in the Medical Department numbered 280,000. This medical force alone was several times larger than the whole Regular Army less than two years earlier. When our country became confronted with the possibility of war and the necessity for adequate National Preparedness the Surgeons General of the Army, Navy and Public Health Service requested of the American Medical Association at its June 1940

President's Address read before the twelfth annual meeting of The Southeastern Surgical Congress, Richmond, March 10, 1941.

session that it undertake a survey of the medical profession with particular reference to the availability and qualifications of its members. The resources of this Association were immediately enlisted through a specially delegated Committee on Military Preparedness consisting of 14 members, 9 of whom serve as committee chairmen for the 9 Military Corps Areas into which the States have been divided by the Army Staff with subcommittees for each State reaching down to the county and district societies, affording complete coverage of the medical profession in the United States. With the cooperation of the Surgeons General of the federal services a questionnaire was formulated designed to elicit the desired information such as age, location, dependents, type of practice, special training, specialty if any, whether or not a diplomate of a certifying board, membership in medical societies, general and special, hospital and teaching appointments, commitments essential to industry, community or state, previous military service and other data upon and from all of which reliable deductions could be made as to qualifications and availability. This is the first time in the history of our country that an effort has been made to classify every physician in the United States according to the nature of his practice in order that proper adjustment can be made under any emergency for the medical needs of the civilian population, the industrial workers and the armed forces. Questionnaires were mailed to 185,797 physicians entitled by registration to practice medicine in the United States and its territories. It is estimated that of this number 145,000 are actually engaged in practice, the remainder having retired because of age, physical disability, or entry into other pursuits. On February 21st 147,670 replies had been received. It was considered necessary to place upon punch cards the information contained in these completed questionnaires in order to make it easily and readily available in various combinations. On the above date this had been accomplished for 136,663 of the completed replies. The purpose of the census is to secure and arrange in useful form complete and accurate data pertaining to all physicians in the United States and its territories. A knowledge of the number, age, location, qualifications, availability and other characteristics of all members of the medical profession is essential in order that the total personnel resources can be utilized in intelligent preparation, appropriate assignment and adequate services for the armed forces, expanding industry and the civilian population.

It is estimated that approximately 7,000 physicians will be required for each 1,000,000 men under arms. Under the present Preparedness Program a force of 1,400,000 is contemplated by

July 1, 1941. This force will include a Regular Army of 375,000, the National Guard of 225,000 and 800,000 selectees.

The present authorized strength of the Medical Department of the Regular Army is 1,230 medical and 267 dental officers. The strength of the National Guard is approximately 1,115 medical and 243 dental officers. This means that about 6,800 medical and 1,600 dental officers must be drawn from civilian and reserve sources The present expansion in the military forces requires additional military hospital facilities to those now existing. In general, 5 per cent of the military population represents the bed requirements in station or camp hospitals and an additional 1 per cent represents the general hospital bed requirement. In round numbers, approximately 84,000 beds will be required prior to the end of the present training year. Of this total 70,000 beds are required in station or camp hospitals and 14,000 beds are required in general hospitals.

The Medical Officers Reserve Corps has an enrollment of 13,861 from which the requirements for the present year may be drawn. The preparedness training envisages a program of five years duration: as it unfolds additional medical personnel will be secured from the physicians of draft age, from further calls upon the Reserve Corps and from voluntary enrollment.

Authority has been given for the formation of sixty general hospitals, thirty evacuation hospitals and twenty-three surgical hospitals or sponsored units. Thus far forty-seven general hospitals, eighteen evacuation hospitals and seven surgical hospitals have been organized.

At present there are on duty in the Navy 886 medical officers, 28 acting assistant surgeons, to which 34 have recently been added, 71 medical officers retired who have been recalled to active duty and 350 medical officers of the Naval Reserve on active duty, making a total of 1,335. All figures are based on a maximum of 500,000 personnel, of which some 400,000 are already on active duty. In the Naval Reserve there are at present 1,763 medical officers, or a shortage of 1,134. There are 300 applications pending.

The cooperation of the civilian profession is paramount in the formulation and completion of the medical effort in this training program, one which the leaders of the nation hope will insure peace but which will insure readiness should the grave responsibilities of war come. Except for the battle casualties the health and medical problems will reach the same magnitude. The medical task is a challenge to the medical profession of the country. The medical profession by education, experience, tradition and moral obligation is prepared to accept now, as it has in the past, the protection of the

health of all the people, whether in the military establishment or in the civilian population. If and when war comes, use of the detailed knowledge of the members of the profession gathered by the Committee on Military Preparedness of the American Medical Association will give some assurance that the individual physicians will be utilized in the departments and in the services for which their training and experience fit them. At the same time it will afford adequate protection for the continuation of service to the civilian population, insure numerical and professional competency to medical school and hospital staffs and prevent the unnecessary disruption of medical personnel from key or essential positions in other phases of civilian life.

The Provision of Service to Industry

The provision of medical service to industry assumes important and difficult proportions. Modern military activity depends basically upon the efficient coordinated industrial production. No other factor associated with the current campaigns has been so forcibly impressed upon our public consciousness. It finds greatest expression in the efforts now being made by our governmental, industrial, labor and military leadership to make available matériel sufficient for the defense of our democratic way of life. In warfare as now waged, the mental and manual work of twelve (to state the proposition conservatively) is necessary to maintain one effective combatant in the field. Loss of working time by indispensable, skilled craftsmen then must be regarded as war-time casualties equal in importance to those which occur in actual combat. The same careful mobilization of medical and hygienic resources will be required to keep them under control. To every physician who indicated active participation in industrial medical activity in reply to the questionnaire of the American Medical Association Committee on Medical Preparedness an additional inquiry has been directed, designed to acquaint the committee with the special qualifications which individual practitioners possess and also certain details about industrial medical facilities which they command. Once these data are collected and tabulated it will be possible to enumerate with considerable accuracy all physicians who have established competency in this field. These for the most part are the men and women who limit their work to or give special attention to one or another of the various aspects of industrial medical activity and who constitute the membership of national and local societies devoted to industrial medicine, surgery and hygiene. It is upon this group that we must depend at the outset, not only to continue their customary services directly applied to the worker, but as consultants, teachers and administrators, local or regional as the emergency requires.

Sufficient information has been accumulated defining quite clearly that actual shortages exist in medical personnel capable of such immediate service. In view of these limitations in qualified personnel, two steps seem practical and logical. The first is that physicians in industry should not be assigned to services of strictly military nature unless special experience, training or previous commitments make such a procedure unavoidable. The other is that it becomes imperative to explore all available opportunities for instruction in the special technics of industrial medicine and hygiene, to the end that an adequate reservoir of well trained physicians and hygienists be regularly available. Physicians working in the industrial field are highly competent in their own special jobs but as far as munitions are concerned they are as a whole untrained. The primary need in the present emergency is an increase in the number of physicians and engineers qualified in Industrial Health and Medicine and their further training in the requisites for control of the hazards of war industries. Among the avenues of approach to the problem being employed are: (a) A survey to determine the present and future needs for men trained in Industrial Health and Medicine: (b) An estimate of the facilities that are now available for training in Industrial Health and Medicine and the development of additional facilities for this purpose, inclusive of the nature of the training that will be required, its scope and length of time. Coordination of the work of the subcommittees on Industrial Health and Medicine and on Medical Education of the Health and Medical Committee of the Federal Security Agency with that of the Council on Industrial Health of the American Medical Association and of the various National Associations of industrial physicians and surgeons: (c) The development and application of measures for protection against occupational hazards. This phase of the work includes questions pertaining to safety measures of various kinds, the solution of toxicologic and engineering problems, the protection against noise, fatigue, etc.: (d) Plans for the promotion of environmental sanitation and other health questions pertaining to housing projects in connection with existing and new industrial plants.

Coordination and Research

With the approval of the President, the Council of National Defense on Sept. 19, 1940 established "as a subordinate body to the Council, a committee to be known as the Health and Medical Committee." This committee consisted of Dr. Irvin Abell, Chairman: the Surgeon General of the Army (Major General James C. Magee); the Surgeon General of the Navy (Rear Admiral Ross T. McIntyre); the Surgeon General of the United States Public Health

Service (Dr. Thomas Parran), and the Chairman of the Division of Medical Sciences of the National Research Council (Dr. Lewis H. Weed).

The order establishing the Health and Medical Committee stated:

> It will be the responsibility of the Committee to advise the Council of National Defense regarding the health and medical aspects of the National Defense and to coordinate health and medical activities affecting national defense. In carrying out its functions, the Committee may (a) utilize, to the extent that such facilities are available for such purpose, the laboratories, equipment and services of the Medical Departments of the Army and Navy, of the Public Health Service, and of other government institutions: and (b) within the limits of the appropriations allocated to it, to contract with and transfer funds to such institutions, and to enter into contracts and agreements with individuals or educational or scientific institutions for studies, experimental investigations and reports.

On Nov. 28, 1940 the Council of National Defense, by executive order of the President, transferred the Health and Medical Committee to the Federal Security Agency, to the Administrator of which, Mr. Paul V. McNutt, was assigned the task of coordination of Health, Welfare, Nutritional, Recreational and other related activities affecting national defense. The special needs in the field of "Health and Medical Care" suggested by Mr. McNutt to the Health and Medical Committee were roughly classified as follows:

1. The need for medical service on the part of both the civilian population and the expanding military forces must be met without detriment to either.

2. Scientific knowledge of medical problems related to defense in both its military and industrial aspects must be extended.

3. Civilian health must be improved in the interest of defense needs, especially among those young men who would be eligible for military service if certain defects or illnesses were remedied, and among those persons whose health is now substandard because of their inability to secure adequate medical care.

4. Population expansion in communities located near large military concentrations and in industrial communities with large defense contracts creates health problems as a result of overcrowding and of inadequate facilities for sanitation, medical care and public health services, including the prevention and control of communicable diseases.

5. Industrial hygiene is an important element in contributing to the productivity of workers in defense industries.

6. Essential medical materials now coming from foreign countries must be assured to meet domestic needs in case foreign sources of supply become un available. This responsibility is shared with the Defense Commissioner in charge of Industrial Materials, who has established a committee to consider this problem.

All of these needs had been under consideration by the Health and Medical Committee previous to its transfer from the Council on National Defense to the Federal Security Agency and certain measures had been inaugurated to meet them, measures which are now being carried out with the aid of the Office of the Coordinator. To fulfil its duties of coordinating health and medical activities, affecting national defense, the Health and Medical Committee appointed six subcommittees which represent large sectors of medical interests. The Subcommittee on Dentistry has, through the American Dental Association, undertaken the listing and classification of all dentists and has under discussion the provision of dental services for the civilian population surrounding industrial centers and military establishments. The Subcommittee on Medical Education has discussed the possible modifications of the Medical Curriculums which may be advisable or necessary to meet an increased demand for qualified medical personnel. It has also been interested in securing deferment of military service for medical students in good standing in approved medical schools and deferment of military service for interns.

The Subcommittee on Hospitals has also considered the status of interns and residents in relation to the Selective Service Law. It has pointed out the need of beds for the hospitalization of neuropsychiatric and tuberculous patients brought to light by the examinations of the draft and induction boards. The Subcommittee on Negro Health considered fundamental health problems affecting the negro, the availability of negro physicians for service with the armed forces and emphasized the need for scholarships to encourage and aid negro medical students. The Subcommittee on Nursing with the aid of the Public Health Service and the American Red Cross is making a national inventory of nursing personnel with the aim of supplying the armed forces with nursing service and at the same time affording continued service for the civilian population. The Subcommittee on Industrial Medicine has been busily engaged with the problems discussed under the heading, Provision of Medical Service to Industry.

The Health and Medical Committee requested the National Research Council to establish committees on aviation medicine and neuropsychiatry as these fields could be more appropriately handled by its Division of Medical Science. The airplane as a technical machine has been developed to a point beyond the resistance of the human machine that operates it, bringing to the fore medical problems for solution. Among these may be mentioned anoxemia; air sickness; fatigue or neurocirculatory asthenia; psychologic and physiologic effects of altitude on the nervous, respiratory and cir-

culatory systems; unusual stresses on the special senses and nervous and cardiovascular systems; effects of cold, wind and speed on the body; multiplicity of tasks; poisoning by carbon monoxide, gasoline or noxious fumes; and protective devices particularly oxygen apparatus. The Committee on Aviation Medicine has made a survey trip of the Army and Navy flying fields and other aviation establishments throughout the country and has made a report on the existing facilities, the research being done and the needs for further development. It will initiate and sponsor research programs looking to the solution of medical problems incident to flying.

Psychiatric and neurologic disturbances take on an added importance during war time. The Committee on Neuropsychiatry is making a thorough investigation of these and related problems such as war neuroses and standards of neurologic disability.

The Health and Medical Committee has made use of the National Research Council's Committees in the special fields of professional advice and research. The National Research Council is the active agent of the National Academy of Sciences and constitutes a democratic organization acting for the great body of scientific men of the United States. It is composed of nine major divisions, one of which is the Division of Medical Sciences, of which Dr. Lewis H. Weed is the Chairman. Under his direction the Division of Medical Sciences has entered into a broad study of the various problems, relating to military medicine. Forty committees and subcommittees, embracing a total membership of two hundred, have been appointed representing various groups and particularly the special societies devoted to the aspects concerned. The members were selected because of their ability and competence in their respective fields and come from twenty-eight different states and the District of Columbia; forty-seven medical schools, the foundations, other institutions, the leading national press associations and a number of governmental agencies have contributed to the committee memberships. The earlier appointed of these committees undertook the investigation and study of specific problems at the request of the Surgeons General of the federal agencies, notably the control of air-borne infections, malaria and typhus; the role of chemotherapeutic and other agents; surgical infections; wound healing; shock, transfusions and blood substitutes. While prosecuting these studies it became apparent that many problems relating to other branches of medicine and pertinent to military affairs could and should be advantageously considered; consequently further committees and subcommittees were appointed until as now constituted they cover most of the special aspects of medical practice and research, particularly as they relate to problems of military

medicine in its broadest sense. It is felt that the general function of these committees of the National Research Council is to give professional advice to the services and to plan and administer research projects essential to the national defense. It happens that some committees by the nature of their interests have confined themselves almost wholly to professional advice while other committees are concerned largely with problems for which there is no immediate answer and which require investigation to supply the information needed. The Committees on Surgery, on Medicine and on Neuropsychiatry of the National Research Council are cooperating with the Committee on Medical Preparedness of the American Medical Association with the aim that in the enrollment of physicians in the expanding military organization they may be so placed that they can render the most effective service. Scientific medicine finds a wide field and an important place in the program of defense and the medical profession may with confidence be relied upon to discharge its duty on a plane compatible with that of a high, patriotic citizenship.

THE PREVENTION OF DEFORMITIES IN COMPOUND FRACTURE TREATMENT

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and
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SOME of the most complex problems encountered in surgery are in those patients who have received compound injuries of the extremities. Until comparatively recent times, the standard treatment of a compound fracture was amputation above it in healthy tissue. During the American Civil War the hospital surgeons amputated practically every extremity in which there was a compound fracture (fig. 1). At the time of World War I the acuteness of this problem caused many effective therapeutic details to be worked out such as proper immobilization with the Thomas splint, routine administration of antitetanic serum, adequate debridement of wounds, and more direct treatment of the fracture itself. Even so, we still see many deformities and untoward complications after compound fractures which make us realize that even better care is needed to reduce the incidence of deformity and disability.

FIRST AID CARE

We consider it axiomatic that splints should be applied to injured patients with a minimum of disturbance of the fragments. A lasting benefit from the first World War was the re-discovery and re-introduction of the Thomas traction splints which in compound fractures of the femur alone reduced mortality rates from 80 per cent to 16 per cent. In general, proper splinting, control of hemorrhage, preservation of body heat and administration of sedatives are essential first-aid measures which should be made available to the injured patient at the earliest possible time.

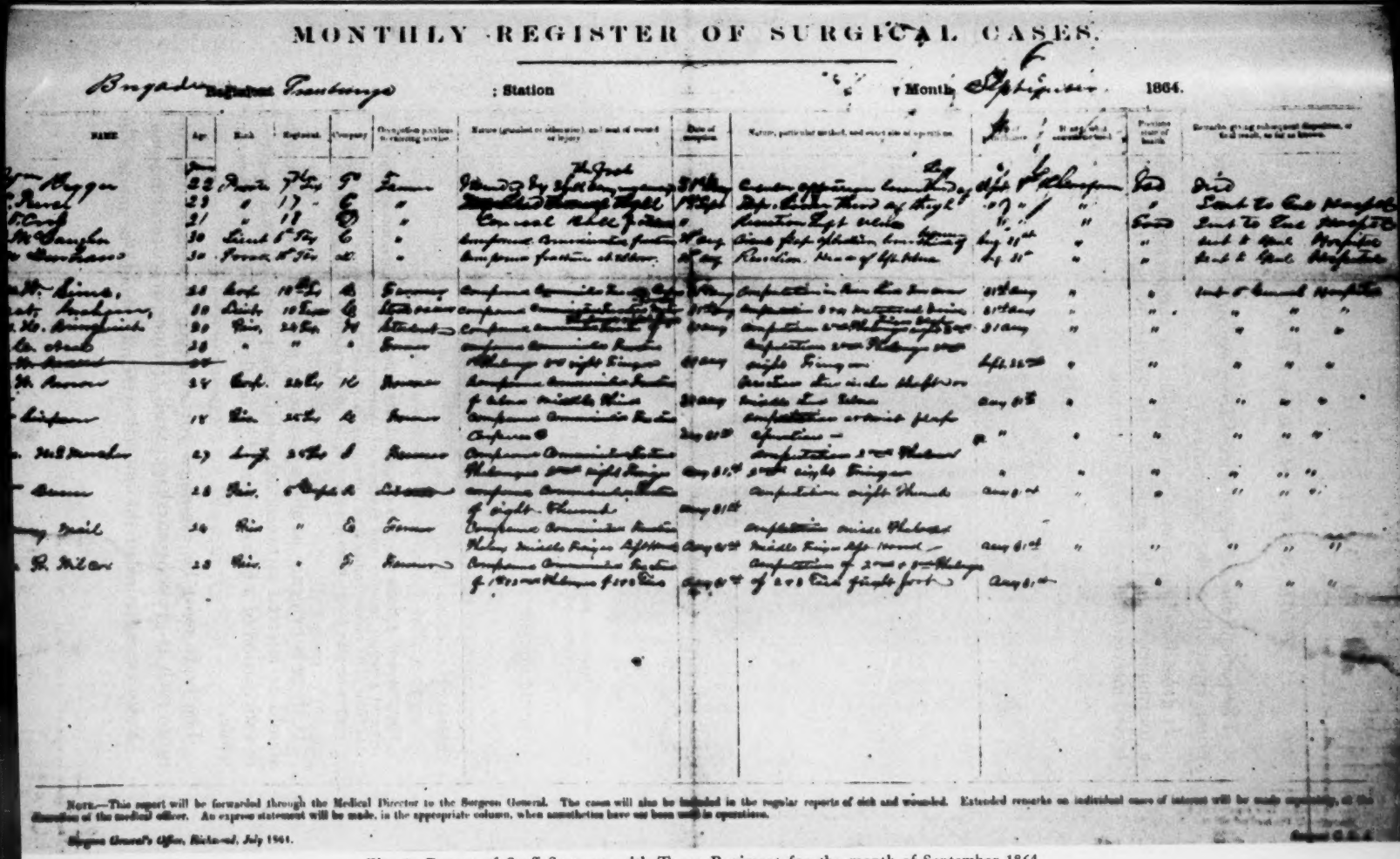
EMERGENCY ROOM CARE

When a patient with a compound injury reaches the accident room at the hospital several indispensable routine procedures must be followed:

The fracture should be temporarily splinted in normal alignment if this has not already been done at the scene of the accident.

Morphine or other sedative should be administered immediately to alleviate pain and to forestall further psychic shock.

This paper was prepared to be presented before the Postgraduate Surgical Assembly of The Southeastern Surgical Congress, Richmond, March 10, 11 and 12, 1941. On account of illness in his family, however, Dr. Stuck was unable to be present.



MONTHLY REGISTER OF SURGICAL CASES.

Brigade Infantry Division ; Station ; Month September 1864.

NAME	Age	Rank	Regiment	Company	Occupation previous to entering service	Nature (gunshot or otherwise), and seat of wound or injury	Date of admission	Nature, particular seat and exact site of operation	Result	If any, date of death	Previous state of health	Remarks giving subsequent disposition, or if a death, as far as known
	Years					The Good						
Wm Boggs	22	Private	7th Tex	G	Farmer	Wounded by a shell passing through	31st May	Amputation of right thigh	Died		Good	Died
[illegible] Reed	23	"	17th	C	"	Gunshot wound of thigh	18th Sept	Amputation of right thigh	Died		Good	Sent to Div Hospital
[illegible] King	21	"	18th	G	"	Gunshot wound of thigh	"	Amputation of left thigh	Died		Good	Sent to Div Hospital
W Langdon	30	Lieut	6th Tex	C	"	Gunshot wound of left thigh	30th Aug	Amputation of left thigh	Died	31st	"	Sent to Div Hospital
[illegible] Cochrane	30	Private	4th Tex	[illegible]	"	Gunshot fracture of thigh	30th Aug	Amputation of left thigh	Died	31st	"	Sent to Div Hospital
[illegible] Sims	28	Corpl	10th Tex	A	Farmer	Gunshot wound of right thigh	31st Aug	Amputation of right thigh	Died	31st Aug	"	Sent to Div Hospital
[illegible] Rodgers	20	Private	10th Tex	G	Student	Gunshot wound of left thigh	31st Aug	Amputation of left thigh	Died	31st Aug	"	Sent to Div Hospital
[illegible] Bumpstead	20	Private	24th Tex	H	Student	Gunshot wound of right thigh	31st Aug	Amputation of right thigh	Died	31st Aug	"	Sent to Div Hospital
[illegible] Cook	28	"	"	"	Farmer	Gunshot wound of right thigh	31st Aug	Amputation of right thigh	Died	31st Aug	"	Sent to Div Hospital
[illegible] Russell	22					Gunshot wound of right thigh	31st Aug	Amputation of right thigh	Died	31st Aug	"	Sent to Div Hospital
W Brown	24	Corpl	22d Tex	K	Farmer	Gunshot wound of left thigh	31st Aug	Amputation of left thigh	Died	31st Aug	"	Sent to Div Hospital
[illegible] Simpson	18	Private	22d Tex	K	Farmer	Gunshot wound of left thigh	31st Aug	Amputation of left thigh	Died	31st Aug	"	Sent to Div Hospital
[illegible] Mc Donald	23	Corpl	22d Tex	I	Farmer	Gunshot wound of right thigh	31st Aug	Amputation of right thigh	Died	31st Aug	"	Sent to Div Hospital
[illegible] Brown	28	Private	6th Tex	A	Farmer	Gunshot wound of right thigh	31st Aug	Amputation of right thigh	Died	31st Aug	"	Sent to Div Hospital
[illegible] Smith	24	Private	6th Tex	G	Farmer	Gunshot wound of right thigh	31st Aug	Amputation of right thigh	Died	31st Aug	"	Sent to Div Hospital
[illegible] Mc Clure	28	Private	6th Tex	F	Farmer	Gunshot wound of right thigh	31st Aug	Amputation of right thigh	Died	31st Aug	"	Sent to Div Hospital

Note.—This report will be forwarded through the Medical Director to the Surgeon General. The cases will also be included in the regular reports of sick and wounded. Extended remarks on individual cases of interest will be made separately, at the discretion of the medical officer. An express statement will be made, in the appropriate column, when anæsthetics have not been used in operations.

Surgeon General's Office, Richmond, July 1861.

Fig. 1. Report of Staff Surgeon with Texas Regiment for the month of September 1864. Note that all compound fractures were treated by amputation.

The patient should be protected from exposure by adequate covering, especially of the extremities.

If gross bleeding cannot be controlled by compression dressings, a tourniquet should be applied to the extremity but it must be released intermittently to prevent ischemia.

Fig. 2, A.—H. J., male 31, deep compound laceration of right forearm with tearing of extensor muscles and fracture of shaft of the radius. Debridement, vitallium plate on the radius and sulfanilamide placed in the wound. X-ray taken two months later shows excellent union of fragments in normal position.

If there is evidence of shock, saline or prepared serum solutions should be injected intravenously while the patient's blood is typed in anticipation of a transfusion. The head should be lowered meanwhile.

The body must be examined for evidence of complicating injuries such as gross hemorrhage, skull fracture or visceral trauma.

X-ray examination of the injured extremity should be made if it

Fig. 2, B.—Lateral view of forearm showing well healed wound, without draining sinus or excess scar. Note range of flexion of the elbow.

can be done without removal of the splint or undue manipulation of the extremity.

Antitetanic serum (1500 units) and anti-gas (perfringens) antitoxin should be administered as soon as conveniently possible. In severe crushing injuries it is advisable to inject larger doses of the combined antitoxin since the danger of anaerobic infections is greater. During the Franco-Prussian War, before the bacteriologic aspects of tetanus were known, there was a 90 per cent mortality from this infection. In the World War, wounded men were injected with antitetanic serum at first-aid stations and the mortality rate was held down to less than 5 per cent.

Debridement of Wound

In the absence of extreme shock (systolic blood pressure below 90 mm.) a patient with a compound fracture should be taken to the operating room as soon as preliminary treatment is completed.

Treatment of shock (transfusion, prepared serum or glucose injection, etc.) and care of the fracture can go on simultaneously without danger if both are done competently.

Whenever possible debridement of the wound should be carried out under general anesthetic so that the muscles will be completely relaxed and the possibility of further pain prevented. The newer

Fig. 3, A.—O. R., male 29, severe crushing compound fracture of elbow due to side-swipe car accident. Wound debrided, loose fragments of bone removed, bone ends reshaped, sulfanilamide powder placed in the wound and the skin sutured. Photograph six weeks later shows skin over elbow well healed with a minimum of scar formation.

and safer anesthetics are less hazardous to older patients or those who are already poor operative risks. Local injection of procaine hydrochloride is not advisable since this may spread contamination or interfere with the impaired circulation. It is safe however to block the nerves of an extremity with procaine when this can be performed a safe distance from the wound.

The skin about the wound must be cleaned with green soap and warm water and be shaved for several inches in all directions. Benzene and gasoline are useful cleansing agents when the skin is very dirty but all such chemicals must be removed with ether. Alcohol or mercresin is then painted over a wide area and the wound draped in the usual manner.

One or two liters of warm physiologic saline solution are irrigated through the wound while all raw surfaces are washed with

gauze sponges. The wound scrubbing should be continued intensively for ten or fifteen minutes. When we realize that the surgeon scrubs his hands for ten minutes before he considers them relatively bacteria-free it is easy to see the inadequacy of a brief perfunctory washing of a contaminated wound followed by a dousing of antiseptic.

Fig. 3, B.—Lateral view of elbow showing range of active motion. In spite of semi-flail joint, patient has fairly good function in the elbow.

All recesses of the wound must be widely opened and examined to insure thorough cleansing. If necessary lacerations are extended by incisions so that no possible cavities are overlooked.

All devitalized or irreparably damaged tissue should be dissected out and removed. Muscle must be trimmed until the tissue is bright red in color, bleeds easily and contracts when pressed with forceps. As far as possible, muscles are cut longitudinally because transverse wounds will not unite well and nerve filaments in the muscle bellies are injured by transverse incisions. Severed nerves and tendons should be sutured except in the case of certain tendons in the hand where the well-developed sheaths make this less successful. Bone fragments should be removed only if they are denuded of periosteum. Bleeding vessels should be ligated but this must be done judiciously to avoid mass ligation of muscle tissue or the use of large quantities of suture material.

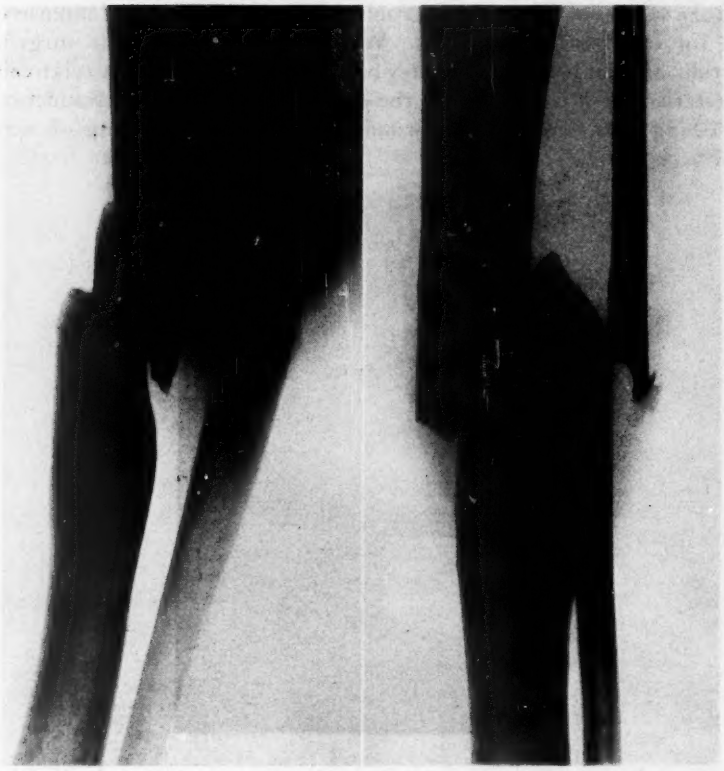


Fig. 4, A and B.—W. H. B., male 71, compound fracture of right leg due to automobile collision. Wound debrided, vitallium plate applied to tibia, sulfanilamide powder placed in the wound, and primary closure. There was no fever or swelling and wound healed with no persistent drainage. X-rays before operation show moderate displacement of fragments.

During the entire process of debridement, instrument technic should be used as much as possible to prevent further contamination. The surgeon's gloves and gowns should be changed frequently, drapes replaced after irrigation of the wound, and fresh instruments utilized in the later stages of the operation.

Care of the Fracture

After the wound has been adequately cleansed attention is directed to the fracture to secure reduction and immobilization in as nearly normal position as possible. Among many commonly used acceptable methods of treating fractures are Kirschner wire traction in a Thomas splint, traction pins incorporated in a cast, and Roger Anderson traction splints, but the decision among them de-

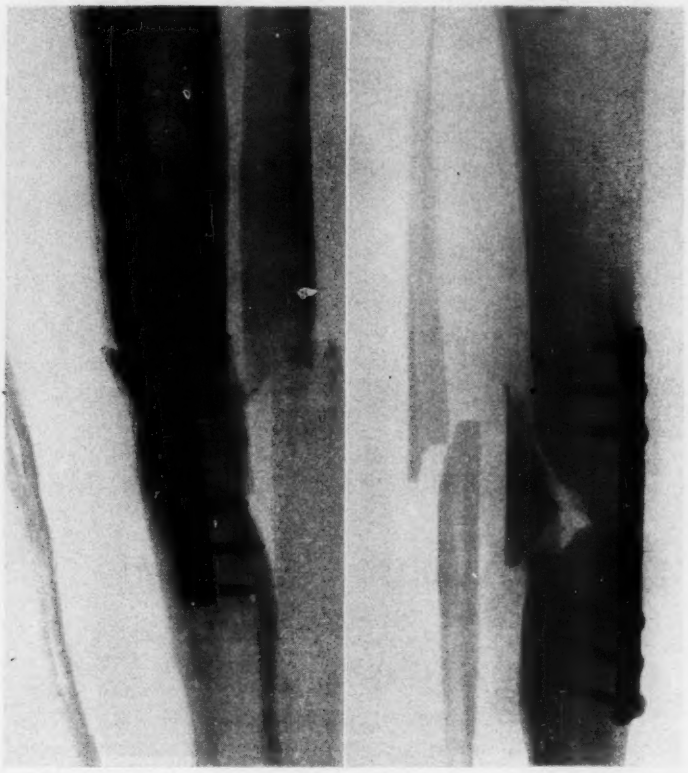


Fig. 4, C and D—X-rays after operation show perfect reduction of fracture of the tibia with immobilization by vitallium plate. Fracture healed solidly in ten weeks.

pends upon the skill of the surgeon, the equipment available, and the ability of the patient to afford long hospitalization.

The use of vitallium plates and screws to immobilize compound fractures now offers hope of more perfect reposition of fragments and consequent earlier union. Plates and screws of other metals were used in the past which caused so much irritation of the bone and aggravation of the infection that this method was criticized and abandoned by most surgeons. Since 1936 when we introduced a passive alloy, vitallium, into bone surgery this field has been reopened because this non-electrolytic metal can be used safely in fresh compound fractures. Moreover the exact replacement and fixation of bones with vitallium plates ensures more rapid healing in the correct anatomic position (figs. 2, 3, 4, 5). After vitallium plates are placed on the bone, the extremity can be supported in a

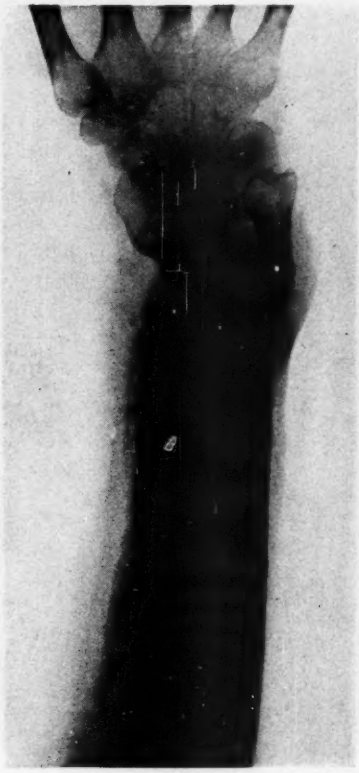


Fig. 5, A.—M. H., female 66, old compound fracture of both bones of the forearm with non-union. Radial fragments freshened, tibial bone graft applied and anchored with vitallium screws. Powdered sulfanilamide sprinkled in wound before closure.

cast and the patient dismissed from the hospital in one or two weeks. With the various traction devices these patients often remain in the hospital for from three to six months.

Wound Closure

Since 1918 Orr has reiterated the advantages of packing infected wounds with vaseline gauze to ensure adequate drainage. Yet even in such wounds, vitallium plates can be used with safety since they cause no erosion of bone and since they will maintain the exact position of the bone fragments.

Recently there has been wide interest in the use of sulfanilamide derivatives in compound wounds. They have been found to retard the development of infections, to act as inhibitors of bacterial

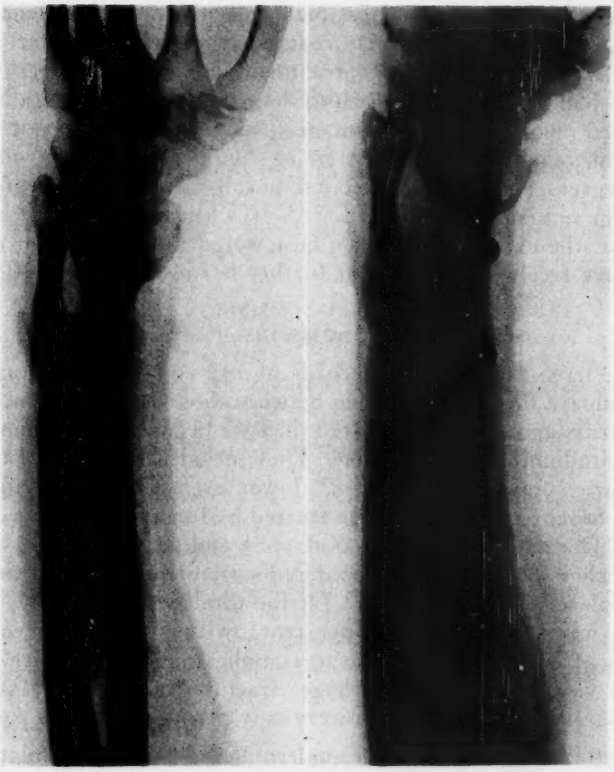


Fig. 5, B.—X-ray three months later reveals solid union of the graft to the radius. Wound healed without drainage and note that bridge of bone has formed across defect in the ulna. The patient has recovered practically normal use of the hand.

growth, and to be very effective against the gas-forming anaerobic bacilli. During the past fifteen months we have used sulfanilamide preparations locally in 69 cases of compound fracture and have been impressed with the marked decrease in subsequent infections. In using powdered sulfanilamide a light sprinkling over the raw surfaces seems sufficient. The use of larger quantities may impede the healing of the fracture and cause unfavorable general reactions although Key and Burford were unable to notice any retardation of healing in experimental animals.

Many compound wounds may be closed loosely with no drains if the treatment is immediate and if debridement is adequate. Nevertheless when a wound is closed, the patient is watched closely for evidence of infection (pain, swelling, fever, etc.) so that sutures can be opened and tension released if these symptoms appear.

One last point of great importance is the need for elevation of injured extremities. Properly reduced fractures or uninfected fractures rarely cause edema if treatment has been prompt. On the other hand, an extremity which has received severe trauma has suffered much circulatory damage. Adequate protection of the circulation requires that the extremity should be elevated from 30 to 45 degrees above the horizontal position to prevent venous congestion and edema. After a few days, when the danger of swelling is past, the extremity can then be lowered and the patient allowed to move freely in bed without further harm to the circulation.

Summary

We have examined the records of 142 compound fracture cases to compare the rate of healing between those we treated more than two years ago and those treated since we began to use sulfanilamide and vitallium internal fixation. They include all the usual types of fracture (upper extremity—52, lower extremity—77, mandible—13). Seventy-three cases were treated by former methods (debridement, Orr pack, skeletal traction, etc.) and sixty-nine cases by modern technic (debridement, powdered sulfanilamide locally and vitallium plates when necessary). Of the total number of 142 patients there were 14 deaths (11 per cent) within the first seventy-two hours after the accident due to complicating injuries such as ruptured viscera, gross hemorrhage, fractured skulls, etc. After the first seventy-two hours there were only two deaths (.016 per cent).

Of the 69 cases treated by modern methods, vitallium plates were used in 35. In this group of patients the wounds healed without drainage in 64 cases while in 5 cases there was some drainage and in two of them osteomyelitis of a mild degree developed. One patient died of septicemia. There was delayed union of the fractures in three cases and non-union in four cases. Sixty-two patients or 90 per cent attained early solid union with no infection, delayed healing, or deformity.

Of the 73 cases treated by former methods there were draining wounds in 12 cases, and osteomyelitis developed in 16. The fractures were delayed in union in 22 cases and non-union followed in 17.

We realize, of course, that comparative statistics must consider the location and severity of the original compound fracture as well as the time which has elapsed after the accident. Yet it is our observation that the modern method of treatment reduces unfavorable complications by more than 50 per cent of those which formerly occurred and deformities are reduced to a bare minimum.

Simultaneous healing of soft tissues and fractures offers the best hope of recovery to the patient and the minimum of disability. Vitallium plates enable reductions to be more perfect and they provide immobilization in the optimum position. This hastens fracture healing and ensures union in normal anatomic alignment.

With this modern method of treatment of compound fractures deformities need not be taken for granted since the problem of infection has been minimized and a safe means of immobilizing the fragments is now available.

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IMMUNOLOGIC PROPHYLAXIS AND THERAPY IN HUMAN STAPHYLOCOCCAL INFECTIONS

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THE etiology and prognostic significance of staphylococci in suppurative processes does not appear to have been materially modified by the recent advances in chemotherapy. Even though these cocci had been previously described, it was not until 1884 that Rosenbach finally established beyond a doubt their etiologic significance. Since this time it has been known that these microorganisms are the most common incitants of active suppurative processes in humans. In view of this it might seem somewhat surprising that such little progress has been made towards preventing their occurrence. Researches by innumerable workers have helped to explain this apparent paradox, by pointing out the fact that in the study of immunity to staphylococcal infection there exists a complex multiplicity of factors many of which are not as yet understood. Since the advent of sulfanilamide and its various derivatives the attention of the clinical as well as the scientific investigator has been diverted towards a study of the therapeutic value of these drugs in infectious diseases. Should sulfathiazole prove to be as effective in staphylococcal infections as it is hoped, the problem of preventing the occurrence of these infections continues to exist, for it has been repeatedly shown that these drugs do not confer an immunity. It is by increasing the individual's resistance to the staphylococci that the prevention of these infections can hope to be accomplished.

Staphylococci are considered opportunists and rely on a break in the host's defense mechanism before assuming their parasitic role. Once a virulent organism has gained access to the deeper tissues which are more susceptible to the toxins liberated by their metabolism, an infection inevitably results. As it is not only impracticable but also impossible to prevent the introduction of these organisms to the more vulnerable tissues, the study of the prevention of these infections has been towards increasing the resistance of these tissues, as well as towards increasing the resistance of the body as a whole.

The ability to resist an infection actually constitutes that which is commonly known as immunity to that particular infection. It is, therefore, obvious that immunity is not only specific but also a quan-

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titative phenomenon. In general terms there are two types of immunity; natural and acquired. The proof of individual natural immunity to staphylococcal infections has not been clearly established. As to the susceptibility to staphylococcal infections, humans may be grouped as either: (1) those individuals that are easily infected and suffer from either chronic or frequent recurrences of infections due to staphylococci, or (2) a more fortunate group who under ordinary circumstances apparently never have pustules, boils, abscesses or other manifestations of staphylococcal disease. It might be said that the latter group possesses an increased resistance to the ordinary exposure to staphylococci or that the former group has a lowered resistance. Even though this increased resistance to infection exists in certain individuals, it does not necessarily follow that these same individuals have been endowed with a natural immunity to staphylococcal infections.

In a study of natural immunity to staphylococcal toxin, Bryce and Burnet[1] determined the antihemolysin titer of individuals ranging in age from birth to the seventh decade. They found that the titer at birth was slightly higher than that found in the serums of normal adults and was equal to and in many instances higher than that in the mother. The titer rapidly fell reaching its low point at eight weeks of life following which time there was a gradual and progressive increase in titer as the years advanced. Using skin tests, Kobak and Pilot[2] made observations on mothers and infants simultaneously. They found that of the 46 mothers and babies tested with both staphylococcal filtrates and vaccines, the majority of mothers gave positive reactions whereas the children gave little or no response which they interpreted as indicating a resistance of the infant to skin test doses of staphylococcal filtrates and vaccines. They also found in a series of 82 infants between the ages of one week and one year, that in general there was very little response to the test in the first few months of life but that there was a subsequent increase in the proportion of positive reactions to the end of the first year. If one is permitted to assume that the negative response to skin tests with filtrates and vaccines as well as the elevated antihemolysin titer in infants is a measure of immunity to infections by staphylococci, it then follows that infants are in many instances endowed with this increased resistance but rapidly lose it during the first few months of life.

In a study of 1062 normal adults who were free from staphylococcal infections Afremow and Pilot[3] found that 417 (39.2 per cent) reacted positively to skin tests with staphylococcal filtrates, whereas of the 56 patients with staphylococcal infections, 49 (87.5 per cent) had positive skin reactions. Comparably similar results

were observed when vaccines were substituted for the toxin. They[4] were also able to show that the skin reactions from broth filtrates were not only neutralized by the serums of rabbits and horses which had been previously immunized with the toxin but were also neutralized by the serums of patients who did not react to the skin tests. Connor and McKie[5] studied the antihemolysin titer in 146 normal persons ranging in age from 11 years to 78 years and found a slightly lower antihemolysin titer than in a control series of patients with staphylococcal infection. Blair and Hallman[6] also found the antihemolysin titer of normal humans slightly lower than in controls, whereas Dolman[7] found that patients with staphylococcal infections had a lower antihemolysin titer in their serums than did the normal humans. Even though these reports seem to indicate that normal adults possess certain specific antibodies for staphylococci in their serums and tissue fluids, it does not necessarily mean that normal adults possess an immunity to these organisms.

The pathogenesis of staphylococcal infections continues to remain obscure. It has long been thought that the virulence of the strains of pathogenic cocci depend to a great extent upon the toxins produced by these strains. The toxic properties of filtrates of cultures of staphylococci were described many years ago. Van de Velde[8], in 1890, observed the destruction of white blood corpuscles by leukocidin. The dermonecrotic effect following the intradermal injection of staphylococcal filtrates in rabbits was reported in 1899 by von Lingelsheim[9]. In 1900, Kraus and Clairmont[10] reported the hemolysis of mammalian erythrocytes in cultures of staphylococci, and in the same year Kraus and Pribram[11] observed the killing of rabbits by the intravenous injection of staphylococcal filtrates. The coagulation of plasma by cultures of staphylococci, a property now used as a test for pathogenicity of strains, was first described by Loeb[12] in 1903.

From the time of these early observations until the investigations of Parker[13], in 1924, which demonstrated the dermonecrotic and lethal effects of staphylococcal filtrates, only occasional reports were made. Recent work indicates that most if not all of the pathogenic strains are capable of producing toxins, whereas only a very few if any of the non-pathogenic strains possess this property. Also Burnet[14] has shown that the production of toxin by various strains of pathogenic staphylococci varies with the type of medium used, the *p*H of the medium and the oxygen tension under which the strain is grown. The estimation of the pathogenicity of staphylococci by their ability to produce a pigment likewise has been shown to be erroneous by Burnet[14], Bigger et al.[15], and Burky[16], who found colony variants of albus in their pathogenic strains. Burnet[14] also

showed that the albus variants give rise to moderately stable cultures which are capable of producing hemolysin in broth. Pinner and Voldrich[17], however, observed that the yellow pigment producing strains were more pathogenic than the white strains.

Following the suggestion by Darányi[18], in 1926, that pathogenic strains coagulated plasma while non-pathogenic strains failed to do so, Chapman et al.[19] studied 5,000 strains of staphylococci and found that the coagulase test is not only an adjunct to the hemolysin test in determining the pathogenicity of strains, but also that pathogenic strains give a positive coagulase test regardless of their hemolytic activity. They also found that the coagulase positive strains are usually pathogenic regardless of the color produced on solid mediums. In 1933, Menkin[20] suggested that the localization of a staphylococcal infection might be due to the fibrinous closure of the surrounding lymphatics and tissue spaces by the production of coagulase. Further investigations by Menkin et al.[21] indicate that staphylocoagulase evidently plays no part in inducing prompt mechanical obstruction to lymph flow. Cruickshank[22] found that the staphylocoagulase determination was a more accurate test of pathogenicity than were other cultural tests. At present the relation of staphylocoagulase to the pathogenicity of strains isolated from human infections is being more critically investigated and premature conclusions seem to confirm the findings of Chapman et al.[19] and Cruickshank[22].

In 1933, Duran-Reynals[23] described a "spreading factor" which invasive strains of staphylococci either possess or can elaborate. His observations[24] indicate that this "spreading factor" is not specific but would enhance bacterial lesions of other organisms including the vaccine virus. The part which this "spreading factor" plays in infection is not clearly understood. It was noted that bacterial lesions were enhanced by this factor when the organisms were introduced in numbers above a certain minimal effective dose and totally suppressed when it was less than this. In animals immunized against the specific test bacteria, it was found that this factor totally suppressed the development of the lesions by the dispersion of the bacteria.

The rationale for the therapeutic use of staphylococcal vaccines in the prophylaxis and therapy of staphylococcal infections dates to the investigations of Pröscher[25] in 1903. Pröscher was able to protect rabbits against the effect of the intravenous injection of 0.5 c.c. of a broth culture of virulent staphylococci by the subcutaneous injection of 1.5 c.c. of immune goat serum. Kitching and Farrell[26] in a series of animal experiments found that immunization

with staphylococcal or formalinized vaccine offered little or no protection to rabbits injected intravenously and subcutaneously with either virulent staphylococci or their toxins. Agglutination and antihemolysin tests on the serums of rabbits immunized with vaccines showed a marked elevation of the agglutinins with no or only a negligible rise in the antihemolysin titer. The agglutinin titer reached its maximum between the sixth and eighth week after starting the immunization with the vaccine. At the tenth week, i.e., four weeks after completing the course of injections, the agglutinin titer had been reduced by one half. Experiments by Downie[27] confirmed the findings of Kitching and Farrell[26], that immunization of rabbits with washed vaccines did not protect the animals against the development of lesions following the injection of living staphylococci.

The anticipated success which attended the early enthusiasm of vaccinotherapy of both chronic and acute staphylococcal infections in humans has in many instances failed to materialize. This does not mean that vaccine treatment of these infections has been a complete failure, for there are innumerable reports of the successful use of this form of treatment. However, the results have not been uniformly good and almost every series reported includes a high percentage of clinically poor results. The failure of Downie[27], Kitching and Farrell[26], and others to protect animals against subcutaneous and intravenous injections of virulent staphylococci by immunization with formalinized and heat-killed vaccines is corroborative evidence that the simple development of agglutinins, precipitins and opsonins is not sufficient to prevent the parasitic action of these bacteria. Julianelle, Wieghard and co-workers[28-31], in studying the immunologic specificity, found a carbohydrate fraction of pathogenic staphylococci which differed from a similar carbohydrate found in non-pathogenic strains both in optical rotation and type of polysaccharide produced on hydrolysis. The serums of rabbits inoculated with whole cocci reacted specifically to a high titer with the specific polysaccharide of the immunizing cocci when tested by the precipitin method. These same authors also demonstrated a complex protein molecule which was species specific. Serologic tests showed that the protein was responsible for the species-specificity whereas the type-specificity was determined by the polysaccharide substances. From these and other observations they have classified pathogenic staphylococci as those containing Type "A" polysaccharide and the non-pathogenic strains as those possessing Type "B" polysaccharide. Both experimentally and by skin-testing[32] individuals they have shown that it is not only difficult to induce specific circulating precipitins but that specific precipitins can be de-

tected only when the infection is severe, prolonged or generalized, and only in those eventually recovering from the disease.

Lyons[33], in 1937, demonstrated the antigenic specificity of the serums of rabbits immunized with heat killed young cultures. Preliminary experiments showed the presence of capsules in three hour infusion broth cultures and that capsules were not present in older cultures. Rabbit serums, containing type specific agglutinins, sensitized encapsulated organisms for phagocytosis and thus allowed the immunized rabbits to clear their blood stream of intravenously injected staphylococci more efficiently than normal rabbits.

The therapeutic use[34-36] of stock vaccine in acute staphylococcal infections has little rationale for its support. The failure to protect laboratory animals should suggest that even though agglutinins, precipitins and opsonins develop following immunization, these antibodies are not sufficient in themselves for protection. There is no evidence that such a mechanism is more effective in humans than in the animals studied. The development of these antibodies takes time and consequently the individual either succumbs or overcomes the infection before a titer of protective or therapeutic value is attained. Also recent investigations indicate a type specific relationship of antigen and antibody which, if it exists, suggests that immunization against these infections will have to be equally specific. In the prevention of recurrent infections the situation is different in that time permits the possible preparation of a type specific vaccine for each case. Early reports by Julianelle[37] on the treatment of staphylococcal septicemia with his type specific Type "A" antiserum show a survival of only 41 per cent which though reasonably good is no better than reports in which other forms of therapy have been used.

Kinsella[38] in his reference to Theobald Smith states: "Those bacteria which act only through their toxins are most easily kept in check." Even though the various factors concerned in the development of a staphylococcal infection are only partially understood there has accumulated a great deal of experimental and clinical evidence that the various toxins may play a major role in their development. Since the early observations on the actions of these toxins, Parker[13], Burnet[14], Panton and Valentine[39], and many others, have made exhaustive studies of the properties of the various toxins produced by these organisms. These workers have not only confirmed the presence of a hemolysin, dermonecrotoxin, leukocidin and lethal factor but have also demonstrated that these toxins are antigens and that serums obtained from immunized animals are capable of neutralizing the various toxins both in vitro and in vivo. This

protection against the toxins of staphylococci is both active and passive. Kitching and Farrell[26] and Downie[27] have shown that even though animals immunized with toxoid may succumb to intravenous injections of virulent staphylococci, this method of immunization offers considerably more protection to the animal than does vaccine immunization.

There exists some disagreement as to the pathologic and antigenic significance of the various toxins. The proportion of each of these toxins in any given filtrate varies with the strain from which the filtrate is produced. Likewise the antibody response in serum of animals immunized with subcutaneous injections of toxins or toxoids varies somewhat as to the proportion of the various toxins in the immunizing filtrate. Some are capable of developing an antiserum with a high anti-leukocidin titer and a relatively low antihemolysin titer, while the filtrate from a different strain might stimulate the production of an antiserum with high antihemolysin titer and a low anti-leukocidin titer. Even though toxins and their toxoids of the various strains studied stimulate the production of all the antitoxins in the antiserum the proportion of these antibodies will vary with the proportion of the specific antigen present in the filtrate employed.

In 1932, Burnet and Freeman[40] showed that it was possible to detoxify filtrates of staphylococci without destroying the antigenic properties of the filtrate. These detoxified filtrates, when injected subcutaneously into rabbits, stimulate an antibody response in the rabbits' serum which is not only measurable in vitro by neutralization tests but also offers a high degree if not complete protection to the animals which are injected with lethal doses of either toxin or virulent staphylococci. The protection against the toxin is practically complete but experiments by Forssman[41] suggest that this protection may not be as complete against virulent organisms. He was able to demonstrate that even though the immunized animals were protected against the immediate action following the intravenous injection of living virulent staphylococci, they later succumbed and in many instances showed localized vertebral abscesses. Similar experiments by Downie[27] and Kitching and Farrell[26] also indicate that rabbits immunized with toxoid have a much higher degree of protection than rabbits immunized with vaccines against injections of virulent staphylococci. However, they confirmed the observations of Forssman in not being able to protect the animals completely.

The tremendous volume of experimental work which has appeared in the literature, points to staphylococcal toxoid as the most

effective method of elevating the antitoxin titer in rabbits' serum as measured by the antihemolysin test. A similar elevation of the antitoxin titer following subcutaneous injections of toxoid in humans has been found by Whitby[42], Murray[43], Buchman[44], and Blair and Hallman[45]. These and other investigators[46-53] have studied the effect of toxoid in the treatment of chronic and recurrent staphylococcal infections including those of the soft as well as of the osseous tissues. Their reports indicate a favorable clinical response. In disagreement with these reports are the observations of Kindel and Costello[54], and Cornbleet and Rattner[55] who failed to observe good clinical results in their cases.

A recent study[56] conducted at the Columbia Medical Center in New York City suggests that in specific cases this form of therapy might prove of benefit. The 35 patients in this series were treated with a concentrated pepsin digest toxoid. This digest toxoid not only proved superior to formalinized toxoid antigenically, but also was more innocuous in that it was found possible rapidly to increase the dose without danger of a systemic reaction; only an occasional mild local reaction occurring. This has a distinct advantage over the formalinized toxoid in that it is apparently safer and the immunizing course of much shorter duration. Hemolysin determinations were made prior to the injection of toxoid and at various intervals during the course of treatment and in some cases after the toxoid course had been completed. As others have previously noted it was impossible to correlate the clinical results with the antitoxin response, some of those showing a good antihemolysin response were clinical failures whereas others with a poor serologic response appeared to be clinically benefited.

The 35 patients presented seven different manifestations of staphylococcal disease which for practical purposes can be grossly divided into two divisions: (1) those involving bone, and (2) those involving only soft tissues. The cases of chronic osteomyelitis failed to show an immediate clinical response in spite of marked elevation of antihemolysin titer in the serum. It is important that these patients be followed over a longer period of time before a correct evaluation of this form of treatment in chronic osteomyelitis be made. Of the 25 cases with soft tissue lesions, 18 showed definite improvement or were cured; in 3 cases the infection did not appear to be modified by the toxoid whereas there were 4 cases which had definite recurrences of their lesions. From these results it might be concluded that in specific cases toxoid therapy is of distinct advantage but that it is impossible to predict or select the cases in which it is likely to be of benefit. As this form of therapy carries a minimal risk and may in specific cases of chronic or recurrent

staphylococcal infections be of distinct benefit, it should prove a valuable adjunct in the treatment of these infections.

It has been shown both experimentally and clinically that it requires several days to develop antibodies in response to the stimulus induced by specific antigens. In view of the fulminating nature of severe staphylococcal infections, the rapid neutralization of circulating toxins plus the clearing of organisms from the blood stream should be accomplished as soon as possible. Studies of the protective value of antiserums developed by bacteria as compared to antiserums developed by immunization with toxin or toxoid, suggest that the antiserum with high antitoxin titer has the greater protective value for animals. Neither antibacterial nor antitoxic serum has been shown to modify the course of the infection in the disseminating focus. From this it would appear that one of the functions of antiserum is concerned with either clearing the blood stream of circulating organisms or neutralizing the circulating toxins liberated by the bacteria. Lyons[57] states: "Type-specific anti-bacterial antibody probably favors the clearance of bacteria from the blood stream but it does not necessarily influence the course of the distributing focus favorably." The more rapid clearing of the blood stream by antibacterial antiserum minimizes the opportunity for the development of metastatic abscesses in cases of staphylococcal septicemia. In those cases in which the toxic features of the disease appear to be paramount, antitoxic serums, as neutralizing agents, should prove of more value than the antibacterial serum which has a very low titer of antitoxin. At present there are no reports of the clinical use of the combined anti-bacterial-antitoxic serums. This should offer an interesting field of investigation.

Encouraging reports from the use of antitoxin in cases of acute staphylococcal infections and septicemia have appeared recently. Panton, Valentine and Dix[58], using a concentrated antitoxin in a series of 13 cases of severe staphylococcal infections concluded that antitoxin was a valuable adjunct in the treatment. Dolman[59] in 1934, reported the use of antitoxin in 104 cases of staphylococcal infection with a mortality of 57 per cent. He emphasized the importance of an early diagnosis with prompt institution of antitoxin treatment, because, in his opinion, the value of antitoxin lies in the neutralization of circulating toxins which are inhibiting or retarding the other body defenses.

Stookey, Scarpellino and Weaver[60] found that 90.1 per cent of the strains of staphylococci isolated from acute infections produced a toxin and because of this, recommend the early institution of antitoxin therapy in cases of staphylococcic septicemia and tox-

emia. Joyner and Smith[61], and Baker and Shands[62] strongly advocate the use of a concentrated antitoxin in cases of acute hematogenous osteomyelitis due to staphylococci. From their investigations they conclude that the neutralization of inhibiting circulating toxin results in a general systemic improvement plus a shift in the white blood count characterized by an increase in the percentage of young polymorphonuclear cells as well as an actual increase in the numbers of leukocytes. More recently, Sutherland[63] stressed the importance of giving antitoxin not only early in the course of the disease but also in very large doses; in his series the total dose ranged from 300,000 to 1,000,000 units. On the Tulane service at the Charity Hospital in New Orleans, we have, in selected cases, administered 20,000 to 40,000 units of antitoxin intravenously as soon as the diagnosis of acute staphylococcal infection is made. This initial dose is, in most instances, given prior to any surgical procedure and it is our impression that antitoxin at this time is of benefit. This is particularly true in cases of acute hematogenous osteomyelitis. The size of subsequent doses varies with several factors; such as age and persistence of toxic symptoms. In general, it has been found best to administer antitoxin at 12 hour intervals in doses ranging between 20,000 and 40,000 units until the clinical picture indicates progressive improvement. As these patients also received other forms of therapy in addition to the antitoxin, no attempt will be made to evaluate separately the clinical effect of any part of the treatment in these cases. However, it might be added that in this series, which is to be reported at a later date, there have been no fatalities.

Experimental and clinical investigations of the antigenic properties of bacteriophage are far from conclusive but indicate that part of its therapeutic action may depend upon these properties. Experiments by Weiss and Arnold[64], Smith[65], MacNeal, Frisbee and Slavkin[66] indicate that bacteriophage not only increases phagocytosis but also induces an increased leukocytic response in the experimental animal. Arnold and Weiss[67] state: "All the antibodies that can be demonstrated in the blood of an immunized animal after the use of B. typhosus, living, dead, and autolyzed can be found after immunization with phage-lysed filtrates of B. typhosus." Larkum[68] found that the agglutinin response in the serum of humans immunized with typhoid phage was the same as in those immunized with typhoid vaccine; that those receiving the phage developed a higher opsonic index than those receiving the vaccine. Researches[69] with staphylococcal phages lead him to believe that bacteriophage is neither a toxin nor an antitoxin but antigenically more closely resembles a toxoid. Holm, Anderson, and Leonard[70] recently de-

scribed a bacteriophage toxoid which seemed to give better protection against intravenous injections of staphylococci. They feel that this is an improved staphylococcal antigen. However, the efficacy of this preparation in human infections needs further study.

There are innumerable reports of the abundant use of bacteriophage in chronic and recurrent staphylococcal infection; some of which indicate that it has proven of benefit in the treatment of pustular dermatitis[71, 72], furunculosis[72, 73], infected wounds[73, 74], and other staphylococcal lesions[75, 76]. However, the evidence is equivocal and in many instances indicates that bacteriophage treatment in these lesions has no advantages over other forms of specific therapy. The disrepute into which phage therapy has fallen is not entirely justified in that the products used were not only phages to which a preservative had been added, but also were of low potency as measured by the test described by Jern and Meleney[77]. These authors have shown that it is important to use a potent phage in order to obtain satisfactory results, and have recently been using an unusually potent phage which they call "double potency phage." They have found this "double potency phage" satisfactory in the treatment of acute and recurrent staphylococcal infections.

The recent reports of the use of staphylococcal bacteriophage have been concerned almost exclusively with its intravenous administration in cases of staphylococcal septicemia. Dutton[78], in 1933, reported 12 cases of acute staphylococcal infection which were treated with intravenous bacteriophage. Of these 12 cases, 7 had positive blood cultures. In this septicemic group there was 1 death; a mortality of 14.2 per cent. Scott[79] and MacNeal and Frisbee[80] reported a mortality rate of 75 per cent in a series of 100 cases of staphylococcal septicemia which were treated with intravenous staphylococcal bacteriophage. In 1939, Longacre, Jern, and Meleney[81] reported a mortality of 47.2 per cent in a series of 36 cases. This series was divided into two groups, consisting of 15 cases and 21 cases with mortality of 73 per cent and 28.5 per cent respectively. In the first group the dose of phage was considerably smaller and less potent whereas in the second group all of the patients received the "double potency phage" in larger doses. This series clearly illustrated the importance of using not only a potent phage but also using it in large doses. The authors also reiterate the necessity of starting phage therapy early in order to clear the blood stream at the earliest possible time and thus minimize the opportunity for establishing metastatic abscesses. There is no proof that the intravenous administration of bacteriophage in any way modifies the distributing focus with the possible exception of foci in the kidney through which organ the phage is passed into

the urine. The most recent investigation on the use of bacteriophage is that of MacNeal[82] who reported a mortality rate of only 8.3 per cent in his series of 12 cases, all of which were in patients suffering with acute osteomyelitis. Even though the antigenic properties of bacteriophage are not clearly understood, the results of its intravenous use in severe staphylococcal infections indicate that this form of therapy has proven as effective as any of the other known forms of specific treatment. Evidence has been advanced that it is not only the lytic factor of this complex solution which is responsible for its beneficial effects. It must be kept in mind that bacteriophage contains many antigens both specific and non-specific and the part played by these antigens can not be overlooked when evaluating the therapeutic properties of bacteriophage.

Summary and Conclusions

Various factors concerned with the pathogenicity and immune responses in humans to staphylococci and their metabolic products have been discussed. The criteria used in differentiating pathogenic from non-pathogenic strains are not definite, but suggest that one of the most constant differentiating features is the ability of the pathogenic strains to metabolize a toxin in vitro. However, recent investigations indicate that the determination of the coagulase factor might possibly be a more satisfactory method of separating the pathogenic from the non-pathogenic strains.

Living and dead bacteria as well as modified and unmodified filtrates injected subcutaneously and intravenously have been shown to be antigenic. Rabbits immunized by injections of a vaccine are not as well protected against injections of virulent staphylococci as are rabbits which have been immunized either with toxin or toxoid. Also antibacterial serum is not as effective in protecting experimental animals as is an antitoxic serum. However, antibacterial serum is thought to clear the blood stream of organisms more rapidly than an antitoxic serum. Neither of the antiserums has been shown to exert a beneficial or therapeutic effect on the distributing focus.

Clinical experiences with stock vaccines in the treatment and prevention of staphylococcal infections have been equivocal. Serologic studies concerned with the antibody titer following a course of vaccine therapy, show a rise of antibodies which, however, takes days to develop their maximum strength. This delay in the development of antibodies plus recent studies indicating a type-specific antigen-antibody relationship of pathogenic staphylococci may partly explain why stock vaccines have proven so ineffectual in acute staphy-

lococcal infections. With the increase in knowledge and experience with type-specific vaccines and their corresponding antiserums it may be hoped that this form of therapy will be of value in chronic or recurrent staphylococcal infections.

Numerous investigators have shown that rabbits immunized with toxoid develop a high antihemolysin titer in their serum and that rabbits so immunized are fully protected against subcutaneous and intravenous injections of toxin and partially protected against similar injections of virulent staphylococci. Even though an exact correlation between the level of the antihemolysin titer and the degree of immunity conferred has not been demonstrated there is some indication that this immunity increases as does the antihemolysin titer in animals. Attempts to show a similar relationship between the antihemolysin titer and immunity in humans have been disappointing in that it has been observed that clinical improvement in patients with staphylococcal infections can not be correlated with the change in the antihemolysin level which follows the use of toxoid. This form of therapy should find its greatest usefulness in chronic and recurrent staphylococcal infections and even though not contraindicated should prove of little value in the fulminating forms of this disease.

The most distressing types of staphylococcal disease are those with positive blood cultures and those with marked toxic manifestations. In the treatment of septicemia it is important to clear the blood stream of the circulating organisms as rapidly as possible in order to minimize the possibility of the seeding to other organs which results in the development of secondary abscesses which in themselves might serve as distributing foci. Staphylococcal antibacterial serum and bacteriophage are more effective in clearing the blood stream of circulating staphylococci than is antitoxin. However, antitoxin both clinically and experimentally has been shown to possess protective qualities which are more effective in the control of these infections. This is probably the result of the neutralization of circulating toxin by the antitoxin. There is abundant evidence that this toxin is not only capable of causing pathologic changes in various organs but also appears to inhibit the normal response of the body to infection. This neutralization of the toxin by antitoxin should lessen the extent of the pathologic changes in the various organs as well as release the normal body defenses to combat the infection. In order to obtain the maximum benefit of the antitoxin it is essential that this be administered early, preferably by the intravenous route and in large doses.

The mechanism of action of bacteriophage administered intravenously is not completely understood. This complex solution con-

tains various antigens as well as the lytic factors, combined action of which is probably responsible for the good therapeutic results which have been reported. The controversy as to whether or not lysis of bacteria actually takes place in the blood stream has not been settled. In spite of the evidence against lysis occurring in the blood stream, it is probable that the lytic principle of bacteriophage has a significant part in its action, the exact mechanism of which is not known. As with antiserum, bacteriophage should be administered early, in a potent form, and in large doses in order to obtain maximum benefit.

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PSEUDOMYXOMA PERITONEI

From Ruptured Mucocele of Appendix

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THE reported cases of pseudomyxoma of the peritoneum from appendiceal origin are few. A survey in 1934 by D'Aunoy and Fine[1] classed only 90 of the reported cases as authentic. One such was found in the Charity Hospital of Louisiana in a 25 year period. A survey of the records in the Louisville City Hospital, covering the past 10 years, does not reveal a case of pseudomyxoma of the peritoneum from appendiceal origin. Kaufmann[2] collected 10 cases from the literature in 1912, Goette[3] reported 2 in 1903, Kemkes[4] recorded 80 cases from the literature.

The precursor of pseudomyxoma of the peritoneum with origin in the appendix is conceded to be a mucocele (cystic disease of the appendix) of this organ. In 1863 Virchow described the lesion as one of colloid degeneration of the appendix. Rokitansky in 1867 described the condition as one of hydrops of the appendix, reporting 4 instances. It remained for Karl Maydl in 1892 to describe the first clinical observations made of mucocele of the appendix.

The author[5] in 1934 published a report on mucocele of the appendix as the causative factor in an acute obstruction at the ileocecal valve due to invagination of a large mucocele of the appendix into the cecum.

Fraenkel[6] reported the first finding of pseudomyxoma peritonei following rupture of a mucocele of the appendix.

Pseudomyxoma of the peritoneum is not a primary disease of itself, although it assumes the characteristics, not only of an inflammatory disease of the peritoneum, but also that of tumor formations in general, as the epithelial cells from the appendix become implanted on the serosa of the intestine and the peritoneum continue to function and secrete gelatinous material. However, it should be remembered as a rule these epithelial cell group implants do not tend to become invasive or proliferate continuously and without control, nor do the cells differ in a great degree from their previous normal structure and arrangement. Thus one must doubt some malignant attributes which have been ascribed to these cell implants.

From the Departments of Surgery and Pathology, University of Louisville School of Medicine.
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Werth[7] in 1884 described pseudomyxoma of the peritoneum following rupture of a pseudomucinous cyst of the ovary with the deposition of a gelatinous material and implants on the peritoneum.

Elbe[8] from autopsies estimated the incidence of cystic disease of the appendix to be 0.5 per cent, Corning[9] reported that 0.54 per cent of appendices removed by surgery are cystic, Ribbert[10] found 1 per cent, Castle[11] 0.2 per cent of mucoceles of appendix in 13,158 autopsies and Norment[12] reported on 45,000 appendices, surgically removed at the Mayo Clinic with the finding of 36 cysts.

The pathologic process involved seems to be one of slow inflammatory stenosis of the appendiceal lumen, followed by complete or near complete obstruction (fig. 1). Distal to this process of lumen obliteration, the presence of active secreting mucus glands persist with distention cyst formation, the accumulated mucus becomes a jelly-like material which exhibits all the characteristics of pseudomucin. Continued accumulation and pressure results in a thin-walled cystic appendix which may be followed by rupture or perforation with extrusion of the content into the general peritoneal cavity. The original obstructive lesion of the appendix in the mucocele formation may eventuate in a complete separation and rupture of the cystic portion with the resultant deposition of the pseudomucin and implanting of epithelial cells on the peritoneum which continue to produce pseudomucin, engendering the condition of pseudomyxoma peritonei (fig. 2).

Werth[7], in describing pseudomyxoma peritonei, said that the peritoneal cavity may be filled with a gelatinous material, the material being partly free and partly in the form of thick semi-transparent layers lying on, and firmly attached to, the abdominal wall and intra-abdominal organs. The material is not soluble in water and cannot, therefore, be absorbed by the peritoneum.

In the case reported in this communication, the semi-transparent gelatinous material was of amber color, in one large mass and confined to the right iliac region of the peritoneal cavity. The cecum, ileum, posterior and parietal peritoneum and one half of the bladder surface were covered with small epithelial implants with a covering of jelly-like material, the implants or epithelial islets stood out (fig. 3), not unlike minute loops of granulation tissue.

There has been difference of opinion as to the chemical nature of the gelatinous material, some obtaining a reaction of mucin, others of colloid but the majority report a reaction of pseudomucin.

Lejars has concluded that the functioning implants, that is those producing mucus, are adenocystomas. This opinion should receive much respect.

In pseudomyxoma of the peritoneum, the symptomatology presents a bizarre picture, varying from those of a simple appendicitis to that of intestinal obstruction, and has, at times, resembled those of an ovarian cyst. A true diagnosis, before surgical exploration, has been very rare. "In no case is there a satisfactory syndrome in which to base a diagnosis with any degree of assurance." (Seelig[13]).

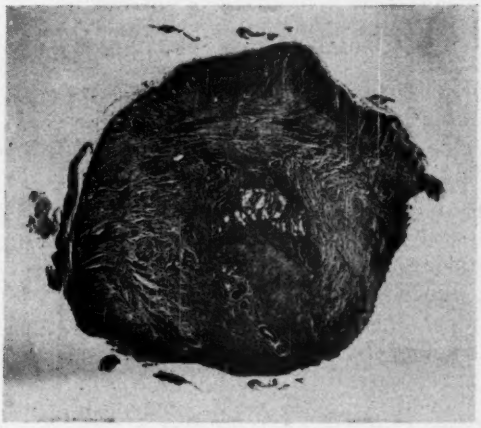

Fig. 1.—Cross section of the distal part of the appendix. The mucosa is absent and the lumen obliterated by connective tissue. The serosa is roughened and a layer of epithelium attached to it.

Clinically, pseudomyxoma peritonei is thought to be fatal, although this has not been universally true as malignant and benign forms are described. The average patient has an expectancy of 4 years but many are living 20 years following operation. Death usually follows acute intestinal obstruction due to the firm agglutination of intestinal loops (fig. 4), which may be progressive, even after repeated operations with complete removal of the gelatinous material, others succumb to sepsis or embolism.

Surgical treatment should include appendectomy for mucocele with removal of as much gelatinous material as feasible, should the implants, in great numbers, be limited to the cecum and ileum, resection of the same should be considered. The complication, which invariably arises in a progressive lesion of this type, is intestinal obstruction: it is in this stage that many patients seek surgical relief. An interesting complication has been reported from pseudomyxoma peritonei of ovarian origin by Hancock and Weeter[14], in which pseudomucin perforated the diaphragm resulting in a bronchial fistula. A similar complication was reported by Peterson[15] in 1919 except for formation of bronchial fistula.

Many surgeons, pathologists and roentgenologists agree that the secreting cells in pseudomyxoma peritonei are not as healthy as before implantation and therefore in this weak state of resistance roentgen therapy offers a satisfactory method of treatment. There are many reports which support this view from a study of end results. It would seem that surgery and x-ray therapy should

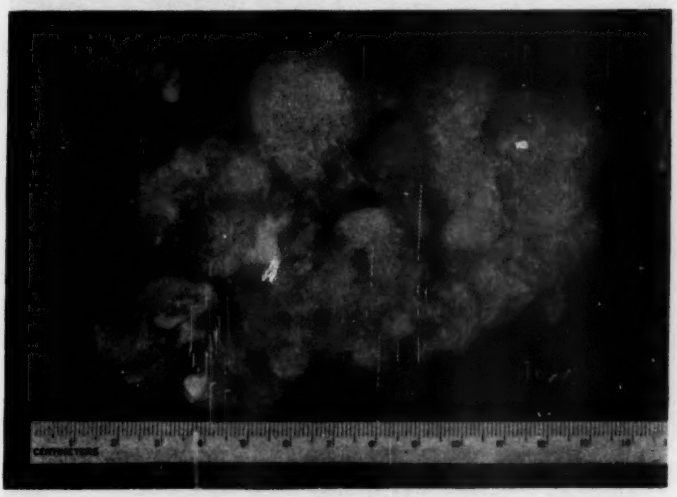

Fig. 2.—The mass of colloid-like secretion containing plaques of organizing tissue and a portion of the appendix.

have a combined field of usefulness in the management of this condition.

The following report of pseudomyxoma peritonei is added to the literature.

Report of Case

A man, aged 54 years, was admitted to the hospital Jan. 19, 1941, complaining of severe pain in the lower abdomen with distention. Eleven hours before admission he had been seized with severe pain in the right lower quadrant of the abdomen, followed by nausea and intermittent vomiting. One year previous a similar attack lasting two days had been experienced.

The abdomen was moderately distended; slight rigidity, with guarding over lower right quadrant, was noted. No absence of liver dulness or abnormal mass was elicited.

The pulse was 90; systolic blood pressure 160, diastolic 90; temperature 99.2.

Erythrocytes 4,170,000, color index .9, hemoglobin 93 per cent; leukocytes 15,500, polymorphonuclears 90 per cent. Urine revealed a few mucous shreds.

Acute appendicitis was recorded as the diagnosis. Under spinal anesthesia

the abdomen was opened through a right pararectus incision, followed by an immediate extrusion of an amber gelatinous mass. On exploration and removal of the jelly-like material, it was found to fill and be limited to the right lower quadrant of the abdomen (fig. 2). Numerous small patches of granulation

Fig. 3.—Plaques of columnar epithelium similar to that of the mucosa of the appendix are attached to the serosa.

tissue like implants were noted covering the cecum, ileum, peritoneum and the right half of bladder (fig. 3). A mucocele of the appendix had ruptured and was free from the distal portion of the appendix. The remaining stump of the appendix impressed one as being patent but no leakage was discovered. The proximal portion of the appendix with mesoappendix was ligated; no attempt was made at inversion. All portions of the mucocyst wall were removed. Two days postoperative a severe diarrhea developed which was controlled by bismuth. Following this there was a good operative recovery. He is now receiving roentgen ray therapy in the hope that some benefit may be derived.

The following is a report on the tissue submitted to Dr. A. James Miller of the Department of Pathology in the University of Louisville School of Medicine.

Gross Description: A portion of appendix and a mass of colloid material (fig. 2).

The appendix is in three pieces, the combined length of which is 67 mm. The distal portion is a solid cord (fig. 1) but the proximal portion has a lumen lined by mucosa. The outer coat is injected and much roughened by adhesions.

The colloid material is 130 c.c. in volume. It is jelly-like in consistency and light yellow in color. Here and there are numerous white flaky masses that have frayed edges, are gray-white in color and are tough. They appear to be connective tissue organization plaques.

MICROSCOPY: In the distal part, the mucosa is absent and the lumen filled in by scar tissue in which there are a few lymphocytic deposits. There is scarring in the muscle and serosa to which a plaque of secreting columnar epithelium is attached. These cells are similar to those of the mucosa of the appendix and are secreting mucus (fig. 3).

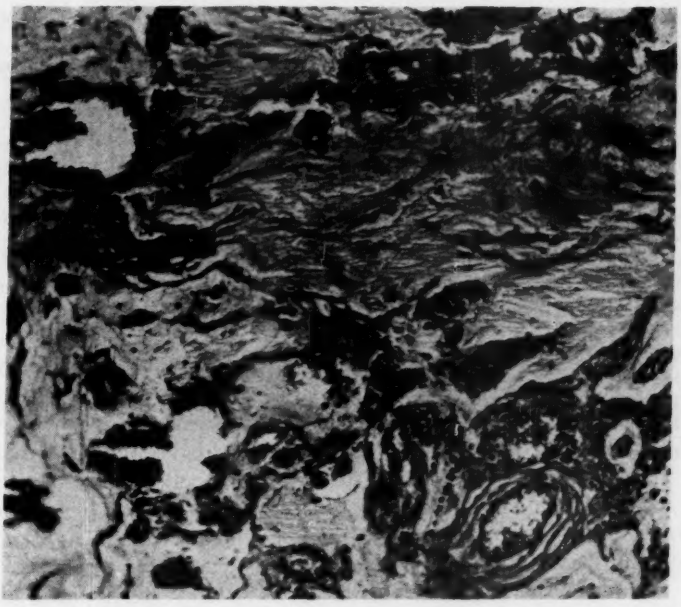

Fig. 4.—A plaque removed from the peritoneum of the parietes. It is composed of much secretion which is being organized. There is a moderate chronic inflammatory reation consisting chiefly of lymphocytes.

Sections of a plaque removed from the posterior parietes is made up of mucoid secretion chiefly. It contains a sparse framework of fibrous connective tissue in which there are islands of mild inflammatory reaction consisting of lymphocytes chiefly. There are a few large cells that appear to be distorted columnar epithelial cells (fig. 4).

The pathologist must consider this condition benign from a histologic aspect but the great number of surgeons consider it potentially malignant, considering the patient's outlook and the high mortality rate incurred. Pseudomyxoma peritonei may be relatively non-malignant but in some instances it follows a carcinoma like pattern.

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CARCINOMA OF THE PROSTATE:
Its Conservative Surgical Treatment

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IT HAS been stated by Wolff that the first case of carcinoma of the prostate recorded as such in medical literature was one observed by Lankstaff in 1817. Beyond any doubt, cases were encountered prior to then but the condition was not recognized pathologically and was grouped along with benign hypertrophy merely as enlargement of the gland. Thompson in 1854 collected eighteen cases of cancer of the prostate and described one he had observed. Wolff in 1899 was able to collect only eighty-three cases from the literature, which made it appear that the condition was not often encountered prior to the turn of the century. However, Albarran and Hallé in a report of a series of cases in which suprapubic operation had been performed said that the incidence of malignant degeneration was 14 per cent; therefore, it would appear that the condition was by no means rare even more than forty years ago. That considerably greater interest in the subject has developed during the past few decades is evident from Kahler's findings. He stated that by 1937 more than 3,100 cases of cancer of the prostate had been reported in the literature. It seems probable that during the past several decades the lengthening of span of life has brought more men to an age at which a tendency to carcinomatous degeneration of tissues might be expected. Greater longevity therefore would seem to be, at least for some, a burden rather than a blessing.

Any estimation of the incidence of carcinoma of the prostate in the whole population is likely to be inaccurate for many reasons. Its comparative importance among tumors of the body is illustrated by a report of von Illyés, who found, based on the statistics of the Metropolitan Life Insurance Company for 1917 to 1928, 1.5 per cent of prostatic cancer in 125,740 cases of cancer of all types. This compares favorably with Randall's findings of an incidence of 1.3 per cent for carcinoma of the prostate in a series of 1215 necropsies. If, however, one begins to restrict his study to certain age groups the incidence appears to be much greater; for instance, Moore found 21 per cent of carcinomas in a series of 229 men more than 50 years of age. His very exhaustive study involved making serial sections of the prostate, which enabled him to find even very small lesions. In most of his cases the lesion could not be recognized

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on gross examination at the time of necropsy. In fact, in only 10 of the 52 cases of malignancy did he suspect it. It is apparent, therefore, that he was not dealing with the lesion which comes to the average clinician's mind when he thinks of cancer of the prostate. The clinical importance of Moore's figures therefore is open to question and my experience certainly would not lead me to believe that the incidence of clinical carcinoma which might affect an individual during his lifetime is anywhere near that great.

It is a certainty that the condition is rarely found among men less than the age of 40 years. In fact, one can almost establish a dictum that malignant lesions of the prostate in individuals younger than 40 years are practically always sarcomas and even these lesions are rare. The disease is most likely to appear, according to a review of the literature including several thousand cases, when the patient is 60 to 69 years of age.

During recent years discussion has been revived concerning the point of origin of carcinoma of the prostate. Opinion is divided; some observers believe that in practically all cases the disease originates in the posterior lobe, and they argue that, if it could be discovered early enough, radical removal of the prostate should afford a very favorable prognosis. Others feel that the malignant process is just as likely to start in the lateral lobes and until it is large enough to produce obstructive symptoms it cannot be detected even by careful digital rectal examination. Kahler, in a study of 195 cases of prostatic carcinoma, found 96 in which the lesion was small enough to be confined to one lobe of the prostate. In 6 per cent of these cases the growth occurred in the anterior lobe, in 48 per cent, in the lateral lobes, and in 46 per cent, in the posterior lobe. Moore in his study of a similar group of cases of small carcinoma found that the anterior lobe was involved in 14.8 per cent, the posterior lobe in 73.5 per cent, and the lateral lobes in 8.8 per cent of cases respectively. The median lobe was not involved in this series of cases. It therefore is apparent that on the question of origin no uniformity of opinion exists.

Predisposing causes of cancer of the prostate sometimes discussed by theorists are of only passing interest. It has been stated that chronic infection, calculi, or unusually large or asymmetrical nodular hyperplasia may predispose to cancer. Kahler compared his series of cases in which necropsy was performed with a control group but could not find evidence to support this theory. Infection was found in 68 per cent of cases in which the lesion was benign and in 63 per cent in which it was malignant. Calculi were found in 3 per cent of the cases in which the lesion was malignant and in 13 per cent of the cases in which it was benign. Marked asymmetry

was more likely to occur with benign conditions than with malignant lesions. Although it has been stated that cancer of the prostate may run through several generations of one family, no really conclusive evidence based on the study of even a reasonably large series of cases has ever been offered. Any theory, therefore, that one might inherit a predisposition to the formation of prostatic cancer or any theory as to the cause of cancer in this organ probably has no real foundation for its advancement.

Metastasis

All of the investigators who have made postmortem studies of cancer of the prostate submit evidence that even in cases in which the primary lesion is very small, metastasis and invasion of structures beyond the prostate are likely to occur early in the course of the disease. Thus, Moore stated, "The further evidence of invasion is the presence of epithelial cells and acini within peri-neural lymphatic spaces. . . . The malignant prostatic epitheilum early acquires ameboid motion and wanders into the lymphatics, since it has been observed in tumors not over 1 mm. in diameter. It is most frequently observed in those tumors which start just beneath the capsule."

Likewise Rich has said, "The tumors were found most often near the outer margins of the gland, and, even when only a few millimeters in size, showed a tendency to invade the capsule."

The size of the lesion in cancer of the prostate is not necessarily an accurate index of its age. For instance, it cannot be stated that a lesion less than 1 cm. in diameter is a week, a month or a year old. The size will vary, depending upon the type of cells which make up the tumor and on other factors, such as the resistance of the patient to the disease. I have seen a number of cases in which a suspicious nodule was felt by rectal examination eight or ten years prior to the onset of the obstructive urinary symptoms which finally required surgical treatment. Furthermore, in many cases a large nodular malignant prostate which has beyond doubt spread to the regional lymphatics may not cause urinary symptoms and may seem not to increase in size for many months. Rich stated, "It is recognized that prostatic cancer is often a slowly growing tumor even after clinical symptoms have appeared and this undoubtedly accounts for the fact that, since the tumor rarely occurs before the age of 50, many of those in whom it has made its appearance die of other diseases of this age period before the tumor causes their death by obstruction or metastasis." One should not conclude that metastasis is an indication of impending disaster. In fact, the evidence clearly indicates that it occurs early but that the cells involved

in the metastatic process, like the parent cells in the original tumor, grow slowly and have no apparent immediate effect on the patient. The eradication of these metastatic cells by surgical methods is, of course, impossible.

Kahler[12] in his study found a very high incidence of perineural lymphatic involvement even in cases in which the lesion was extremely small. In fact, in searching for extension to the perineural lymphatics with the low power objective, such involvement was found in the same microscopic field as the tumor in all except 13 per cent of the grade 1 tumors and in 15 per cent of the grade 2 tumors. Furthermore, he found that in 51 per cent of cases in which the tumors were recognized clinically or grossly distant metastases were demonstrable at necropsy.

These facts are important considerations in determining the proper clinical management. The evidence points to the almost inescapable conclusion that complete surgical extirpation is rarely possible.

Clinical evidence of metastasis, such as positive roentgenograms or palpable regional lymph nodes, according to various observers, occurs in from 25 per cent (Bumpus) to 58 per cent (Barney and Gilbert) of cases, or even more, depending upon the type of cases studied or the groups into which they are placed.

Clinical Diagnosis

There are no pathognomonic symptoms of carcinoma of the prostate. The first indication of the presence of such a growth may be the onset of obstruction to micturition or, on the other hand, no mechanical obstruction to the outflow of urine may develop at any stage of the disease and only when rheumatic pains, sciatica, loss of weight or other signs of metastasis are present does the physician point an accusing finger at the prostate and discover the primary lesion. It is unfortunately true that symptoms which might direct early attention to the prostatic carcinoma are peculiarly conspicuous by their absence. The disease is, therefore, seldom discovered until it is well advanced.

By rectal examination it may be possible to palpate a pea-sized lesion providing it is projecting posteriorly or occurs in the so-called posterior lobe. A similar sized lesion in the lateral lobes would not be palpable. As a general rule, however, one finds a stony hard lesion of some size, often in the extreme lateral borders of the prostate. Oddly enough, the examiner in his diagnostic efforts will sometimes go beyond the growth with the palpating finger and miss the very characteristic woody raised edge of the lesion close to the

anus in the apex of the gland. In still other cases the main portion of the prostate may be soft and it is only by reaching up near the seminal vesicles that one can palpate the malignant portion.

One cannot "go through the motions" of a rectal examination, conclude it in a few seconds and make an accurate diagnosis in obscure cases. Experienced urologists agree that the most reliable method, short of microscopic examination of the tissue, is the carefully executed rectal examination.

It is rarely necessary to employ the needle biopsy in order to arrive at a diagnosis. This method, if it fails to procure malignant cells, reveals little if anything, and in those cases in which an aspiration biopsy is positive there is practically no doubt of the nature of the lesion at the start. I, therefore, have quit using it.

Prostatic calculi or tuberculous disease both cause in some instances extremely hard areas which are difficult to distinguish from a malignant lesion by palpation. One, however, has the assistance of the roentgenogram and of urinalysis in making a differential diagnosis. Clinically, there is rarely any actual difficulty in making an accurate decision.

In rare cases of prostatic cancer the gland feels exactly like a benign gland but the tissue on microscopic examination will prove highly malignant. In these cases there generally is roentgenographic evidence of metastasis when the patient is first examined and often he is suffering with pain due to involvement of the bones and nerve roots. I have seen a number of cases of this type in which the diagnosis was missed at the time of original examination because the prostate did not feel malignant and the physician neglected to make a roentgenogram. Obscure causes for anemia, anorexia, vomiting, loss of weight, headache and a variety of other symptoms can sometimes be found by careful examination.

Only in very few instances is the diagnosis made solely on the basis of the cystoscopic or urethroscopic findings. In such cases the tumor apparently arises high in the lateral lobes and spreads upward to encircle the vesical neck. With a retrograde lens cystoscope one can see small patches of tumor breaking through the mucosa which overlies the trigone and vesical wall immediately surrounding the internal urethral orifice. As a rule the tumor is of high grade in such cases. Biopsy with a small cystoscopic forceps can be employed for confirmation.

Treatment

Colston has stated that in all cases of cancer of the prostate observed at the Brady Institute over a period of fifteen years only 4

or 5 per cent of the patients could be treated by radical operation. He further stated that of all patients thus treated, about 50 per cent lived five years or more. This brings the chance of finding a case in which there is real hope of cure by radical operation down to around 2 per cent or 1 chance in 50, not a particularly encouraging prospect at first glance for the average patient suffering from cancer of the prostate. Colston stressed the importance of careful rectal examination of all men more than 50 years of age, as part of every routine physical examination. With this I heartily agree for it is only by this method that carcinoma can be detected early.

Since some of these patients are at an age when various degenerative diseases of other organs are present, it seems likely that even though the local lesion may be small there are at times contraindications to radical surgical treatment. For instance, a patient aged 70 years, who has hypertension, diabetes and a cardiac complication would not be a fit risk for a radical operation and one would hesitate to advise it for his life expectancy would hardly justify the risk. Furthermore, one must keep in mind that it is possible to contribute to such a patient's further discomfort in view of the fact that in more than half of the cases varying degrees of incontinence ensue following a radical operation. This is an unfortunate fact which to some extent has been remedied by recent improvements in technic.

During the past ten years at the Mayo Clinic we have not employed radical perineal prostatectomy. In our opinion the evidence at hand clearly indicates that when carcinoma of the prostate has grown sufficiently to cause urinary obstruction the disease has spread through the perineural lymphatics and cannot be completely eradicated by a surgical procedure.

It is our feeling, therefore, that adequate transurethral resection, removal of all of the obstructing tissue and the employment subsequently of deep roentgen therapy offers the patient a better prognosis than does any radical procedure. There is much less risk to life and almost certain assurance that control of micturition will be perfect.

It has been stated that transurethral resection is not acceptable as a means of relieving carcinoma of the prostate with complete obstruction for it does nothing to effect a cure. In such cases the same criticism can be made of any other surgical procedure according to the evidence submitted by Moore, Rich, Kahler and others who have studied this subject from the pathologist's viewpoint.

When complete obstruction to micturition has occurred the cancer has already progressed beyond all hope of cure in the broad interpretation of this word. However, it is certainly true that in many

cases all of the symptoms of which the patient complains can be relieved by transurethral resection. He can be restored to apparent health and can resume his occupation. Economically and socially he is again a citizen. With the aid of deep roentgen therapy, regrowth of the prostate can sometimes be postponed. Of course, it is essential to remove completely the tissue which has caused the urinary dysfunction. This can be done adequately by transurethral resection; in fact, there is no limit to the amount that can be excised. Furthermore, the prostatic urethra will heal and the urine will become perfectly clear in almost all cases.

My experience with this method warrants the opinion that it is the greatest boon thus far devised for the treatment of malignant lesions of the prostate. The operation must of course completely remove the tissue which is interfering with the function of the vesical neck. If this is done there will be no ulceration, sloughing or foul urine. These result not from the method but from its poor execution. There is no logical reason why a better functional result can be obtained by either perineal or suprapubic operation. In fact, a more accurate operation can be done by the transurethral route.

The actual technic of transurethral resection has been described in previous articles.

Results of Treatment

In order to present some data regarding our experience with conservative surgical treatment of carcinoma of the prostate I have reviewed the records of 253 cases in which transurethral resection was done prior to January 1, 1936. Five years or more have elapsed since operation was performed in the last case which is included in this series. In a previous article Emmett and I presented data, some of which were quite detailed, concerning 107 of these cases. We found that in the large majority of cases urinary obstruction was completely relieved by the operation and that it did not recur until death occurred either from metastasis or in many cases from other causes, such as heart disease, cerebral apoplexy and senility. In some instances urinary obstruction did recur and it was possible to relieve it again by transurethral resection. In only extremely rare cases was it necessary to relieve the obstruction either by suprapubic cystostomy or by inlying urethral catheterization.

Our experience since then corroborates these early findings. A detailed analysis shows that the period of survival following operation is surprising. It has been alleged that transurethral resection offers the patient who has cancer of the prostate very little and that

the majority of patients will die within a year after operation. Our findings are in distinct contrast to this.

We are in the process of tracing by letters and in some cases by re-examination the 253 patients who were subjected to transurethral resection prior to January 1, 1936. Up to the present time as many as 83 per cent of these patients have been traced at survival periods of one, two, three, four and five or more years. The study is still going on and we expect to trace all the patients just as Emmett and I did in our previous study.

To date, of the traced patients, 74 per cent survived at least a year, 46 per cent at least two years, 31 per cent three years, 17 per cent four years and 8.7 per cent survived for five years or more. This substantiates the statement that the results of transurethral resection for carcinoma of the prostate compare very favorably with those following other methods of operation. In addition, the method has the distinct advantage of a low mortality rate for in the 253 cases there were only two hospital deaths or a mortality of less than 1 per cent.

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OVARIAN HORMONAL HARMONY

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AS STATED in an earlier paper[1], the human ovary is comprised of cells which, combinedly or individually, effect histologic changes during its cyclic phases. Close observation of these histologic changes results in a better understanding of ovarian metabolism. The divisions of ovarian metabolism being anaphase and cataphase.

The anaphase, which commences with the onset of menstruation, is characterized by follicular cell reduplication, estrone synthesis and the formation of a follicular cyst[2]. The vagina and uterus bear evidence of this phase by hypertrophy.

The cataphase commences with the passage of the ovum from, or the death of the ovum in, the follicular cyst. The formation of a hematoma, a fibroma and an interstitial oophoritis in the ruptured follicle are characteristic of this phase. The cataphasic criteria are produced by the remaining follicle cells, those of the theca interna, estrone and blood. The follicular cells, of epithelial origin, contain lipoids of phosphatide and cerebroside types and a lutein, chemically like carotin. The epithelioid theca interna cells, which take origin from the mesenchyme of the urogenital fold, contain cholesterol esters and doubly refracting lipoids.

The elements productive of this phase remain active until the "interstitial" oophoritis stage is reached.

The vaginal mucosa characterizes the cataphase by atrophy. The uterus characterizes the cataphase by secretory endometrial changes (fig. I).

Impregnation of the ovum produces ovarian changes which cause the cataphasic phenomenon to be dominant during the first eight months. From the eighth month to term, anaphasic phenomenal changes are found in the ovary and vagina.

The effect of altering the follicular and thecal relationship is demonstrable experimentally by castration, transplantation and ablation experiments and by the injections of potent ovarian extracts.

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*Dr. Russell, on leave from the University of Tennessee, started collaborating with Dr. Bennett in May, 1940.

Iscovesco[3] illustrated in 1912, by lipoid solvent injections of ovarian extract, a marked hyperplasia of the tubular reproductive tract in the immature rabbit.

Aschner[4] observed in 1913, the hyperplastic effects of lipoid extracts of the ovary on the uterus of immature rabbits.

Shay, Gershon-Cohen, Paschkis and Fels[5] in 1939, report the luteinization of ovaries of female rats, injected with testosterone proprionate.

Allen and Doisy[6] in their study of the follicular hormone, noted its affects upon the uterine and vaginal epithelium. In the monkey, following injections of the follicular hormone, the uterus becomes enormously enlarged and vascular. The developmental changes in the uterus, produced by the estrone, are analogous to those occurring in the menstrual cycle of the monkey during the non-breeding season, when there is an abundance of ovulation and luteinization and the effect on the uterus due solely to the hormone elaborated by the graafian follicle. The cyclic uterine bleeding which, nevertheless, occurs during the non-breeding season, is characterized by an absence of nidatory changes in the endometrium due to the failure of luteinization. The inability of estrone to produce nidatory changes in the endometrium may be demonstrated by curetment of castrated women under treatment with estrone. Estrone is capable, therefore, of producing hypertrophy and vascularization of the uterus, but is incapable of producing the nidatory endometrium.

Injections of potent luteal extracts illustrates the inhibitory action of this hormone upon ovulation. This was illustrated by Papanicolaou[7] in 1926. In his experiment he reported the suppression of ovulation and estrus in the guinea pig, after an injection of an aqueous extract of corpora lutea.

If 21 c.c. of untreated urine, of the hypofollicular individual, is injected into the vein of the isolated, adult, female rabbit, autopsy at the end of 48 hours revealed no alteration from the normal.

When, however, 21 c.c. of the untreated urine from a hyperfollicular individual is injected into the vein of the isolated, adult female rabbit, distinctly abnormal changes are discernible at the autopsy 48 hours after the injection. The rabbit ovaries are follicularly polycystic. Engorgement of tubes and uterus is likewise noted.

The restoration of physiologic function to average in both the excessively and deficiently interstitial ovarian cases by ovarian isoplasty (which entails the exchange grafting of a hyperinterstitial

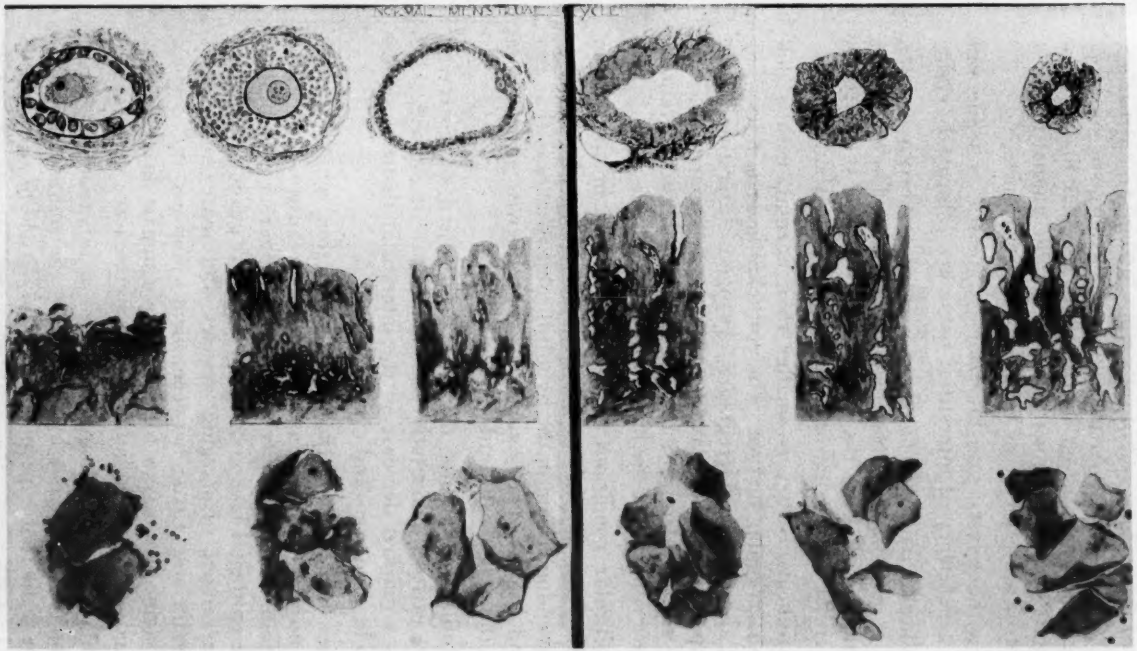

Fig. 1. The normal menstrual cycle showing the commencement of follicular growth dependent on balanced ratio of follicular and interstitial cells. Follicle growth continuous to ovulation. Following ovulation, lutein and estrone act in combination in ruptured follicles. Lutein gradually becoming more dominant as estrone disappears from "luteal" body. The "luteal" reign ends with commencement of next menses.

Endometrium at beginning of follicle growth represented by type found on second menstrual day. From cessation of menses to ovulation it hypertrophies. From ovulation to ensuing menses becoming secretory with large tortuous perpendicular glands.

Vaginal mucosa at origin of follicle covered with many erythrocytes, few polynuclear leukocytes, no bacteria. The cells when smeared on slides show mosaic patterns, thick, granular cytoplasms and gram negative nuclei. *p*H 7. During weeks to ovulation (post-menstrual) no erythrocytes, few leukocytes, myriad diffusely spread gram negative cocci. Cells becoming more numerous and larger as menstruation approaches. Following ovulation *p*H 6, many leukocytes for a few days, gram negative cocci clumps, mosaic patterns of cells disintegrate, cytoplasms thin and granules fade. Cells as the estrone content of "luteal" body becomes less, atrophy. Several days prior to menstruation a "young" type of leukocyte appears in company with myriads of large gram positive bacilli (Doederleins) *p*H 4.5.

and hypointerstitial ovary) conclusively proves the dependence of ovarian normalcy upon hormonal interrelationship[8].

From our experiments and clinical observations, it appears that the products of the follicles and of the corpus luteum, are, in a sense, antagonistic to each other. Actually they are synergistic or cooperative. The synergistic action is shown by the inability of progestin to initiate a progestational condition in the animal unless it is first put into a state of estrus by injection of estrone.

An ovary without cysts, says Hertzler[2], is aplastic or senile, but ovaries with a deficiency of interstitial tissue are follicularly cystic.

In hypofollicular patients (fig. 2), possessed of fibrotic ovaries, there exists a quantitative deficiency of estrone. These ovaries exhibit a general increase in the interstitial tissue. In such ovaries follicles are either obliterated or are represented as small cysts.

The hypofollicular ovary is smaller than normal, with a dull white, grayish, irregular surface. The epithelial layer is thick. The cells are tall, agranular and irregularly arranged. Interstitial tissue encroaches upon the cortical layer. Occasionally isolated graafian follicles are seen. Corpora lutea are rare. Interstitial cellular stroma is more compact at the hilum.

In hypofollicular conditions, the uterus ranges in sizes from slightly smaller than normal to the hypoplastic or aplastic infantile type. The endometrium in the hypofollicular ovaries is thin, undeveloped and friable. The vaginal mucosa is likewise either hypoplastic or of the aplastic infantile type.

In hyperfollicular patients (fig. 3,A) possessed of polycystic ovaries, there exists a quantitative overabundance of estrone. This type exhibits a marked decrease in the interstitial tissue. Follicles are found to be numerous and cystic.

The ovaries in the hyperfollicular types are thin, white in color, larger than normal, with surfaces irregular because of numerous protruding follicles and nearly always are adherent to adjacent organs. The epithelial layer is thin and the flat granular cells are irregularly arranged. Enlarging vesicles and maturing follicles with little connective tissue between them compress the cortical layer. The connective tissue forms a thin compact layer around the vessels and nerves at the hilus. Corpora lutea are very rare.

Uterine enlargements accompany ovaries of this type. In hyperfollicular conditions there is a hyperplasia of the endometrium that may either be a diffused hyperplasia or a localized one of the polypoid form. In either case, the condition exists because of one of two factors. Either the ovary contains very large, atretic follicular

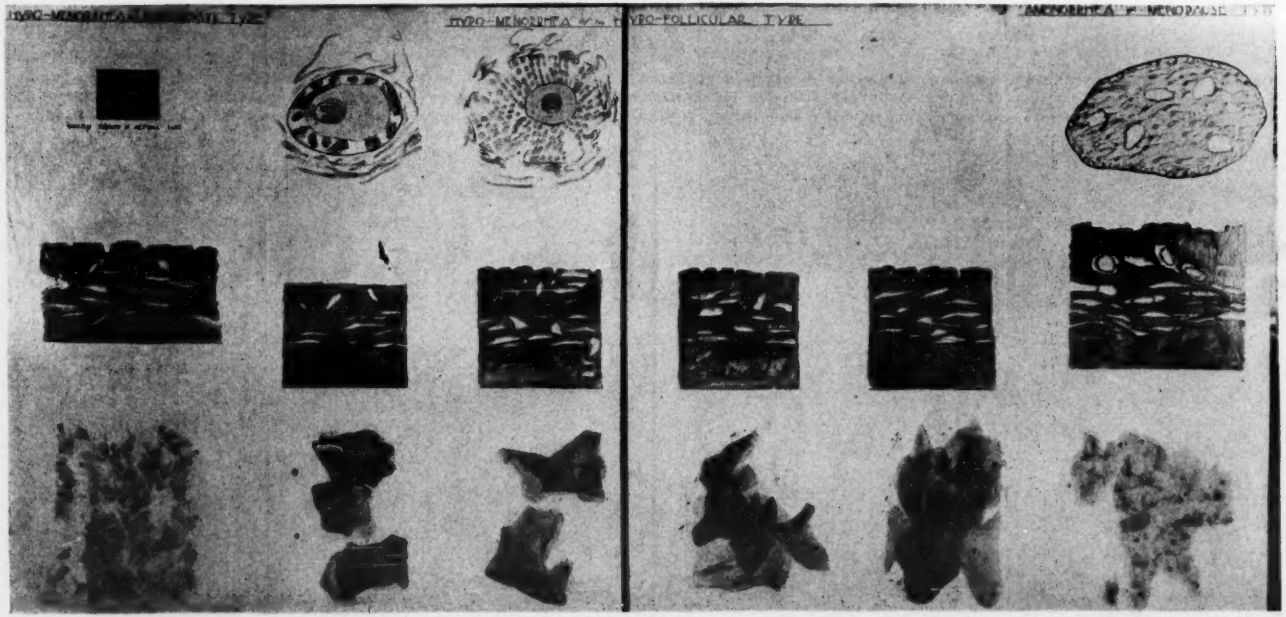

Fig. 2. The hypoplastic type showing an underdeveloped ovary accompanied by a hypoplastic endometrium and a hypoplastic vagina, the mucosa of which shows fairly thin lightly stained cells. *p*H 5.

The hypofollicular type of hypomenorrheic shows a poorly developed follicle with insufficient cells of follicular nature, excessive interstitial cells.

Endometrium section indicate insufficient estrogen formation, thin hypoplastic. Glands mostly parallel with uterine muscle layer.

Vaginal mucosa in menses less atrophic than in succeeding weeks. Erythrocytes occasionally found in menses smear. Gram positive (Doderlein) bacilli appear throughout cycle. These cells are squamous. *p*H 4.53.

Menopausic types are amenorrheic showing ovaries of the "interstitial" type, the follicles represented as cysts.

Endometrium is flat with "thin" glands parallelling the muscular layer of the uterus.

The vaginal mucosa atrophic with many "free" nuclei. Cells as in hypoplastic are mostly stellate with thicker cytoplasms. *p*H 4.5.

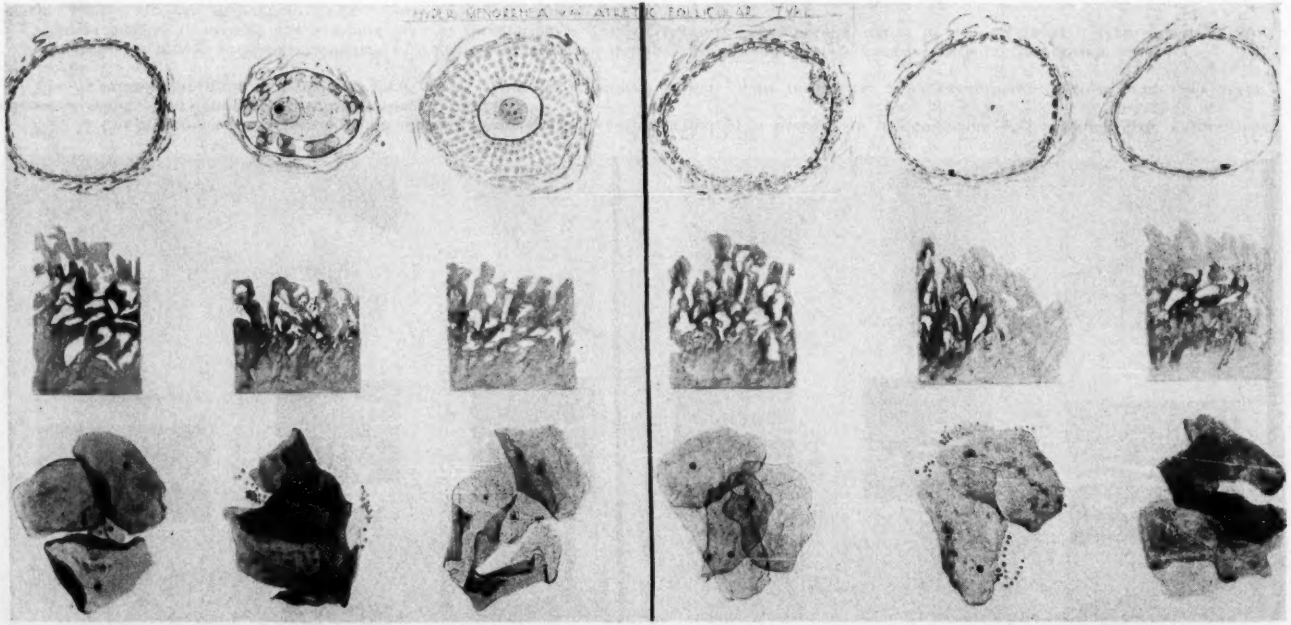

Fig. 3. A. The atretic follicular type is hypermenorrheic, the growth of the follicles associated with deficiency of interstitial tissue. Endometrium is markedly hyperplastic. Vaginal mucosa is hyperplastic, not mosaicly arranged. Leukocytes and erythrocytes may be encountered at any time. Uterine bleeding of menstrual type appears to accompany death of the ovum. Bacteria when found are gram negative cocci. *p*H 6.

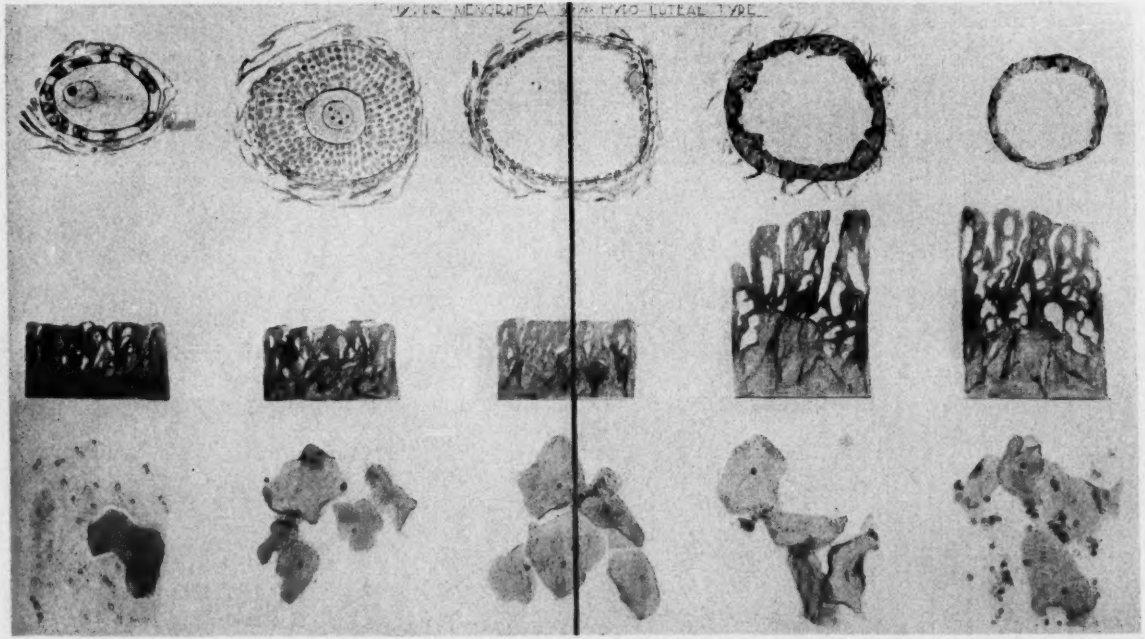

Fig. 3. B. Hypoluteal type, hypermenorrheic, insufficient amount of interstitial tissue in ovary producing excessive estrone following ovulation in luteal body.
Endometrium exhibits prolongation of menstruation but even so a hyperplasia.
Vaginal mucosal changes evidence the follicular and luteal phases of the "normal" but not to the same degree. pH 6 to 5.

Hypofollicular Cases

Case Numbers of Broad Street Hospital, Philadelphia.

1.	2394	12.	1499
2.	595	13.	620
3.	598	14.	2392
4.	1618	15.	1219
5.	1970	16.	1699
6.	2218	17.	1740
7.	2241	18.	4518
8.	2053	19.	2416
9.	1627	20.	1480
10.	1642	21.	2295
11.	1100	22.	1778

Hyperfollicular Cases

Case Numbers of Broad Street Hospital, Philadelphia.

1.	1482	34.	240	67.	637
2.	621	35.	1084	68.	535
3.	1099	36.	1041	69.	510
4.	2328	37.	866	70.	14
5.	2393	38.	829	71.	1264
6.	538	39.	817	72.	1410
7.	1295	40.	730	73.	1411
8.	1281	41.	380	74.	1383
9.	902	42.	265	75.	1179
10.	44520	43.	101	76.	1178
11.	1782	44.	98	77.	1094
12.	1115	45.	1267	78.	1089
13.	2219	46.	1419	79.	1741
14.	H-31	47.	1471	80.	1431
15.	1729	48.	1341	81.	1369
16.	1969	49.	857	82.	811
17.	2050	50.	1836	83.	933
18.	2240	51.	1768	84.	496
19.	2294	52.	1290	85.	364
20.	1824	53.	1167	86.	303
21.	1639	54.	1166	87.	32
22.	1617	55.	1023	88.	1473
23.	1690	56.	1011	89.	348
24.	1702	57.	988	90.	386
25.	1481	58.	891	91.	492
26.	1259	59.	880	92.	692
27.	1115	60.	590	93.	762
28.	668	61.	73	94.	869
29.	350	62.	873	95.	913
30.	42	63.	778	96.	946
31.	83	64.	761	97.	1197
32.	108	65.	643		
33.	209	66.	641		

cysts, or, follicles which upon rupturing, produce an insufficient luteal substance. The vaginal mucosa in these cases is likewise hypertrophic (fig. 3, B).

The ensuing data correlate the ovarian condition with the clinical and physiologic picture. Ninety-seven patients, whose ages varied from 14 years to 54 years, all presented the following type of picture.

The average catamenic history for this group is: menses established at 13 years, recur every 28 days and last 9 days. Gross examination reveals uterine myoma or fibromyomas in company with the hyperfollicular ovaries. The pathologic examination reveals cystic graafian follicles, myoma of the uterus with some calcareous deposits and hyperplasia of the endometrium. Only in the clinical diagnosis did these 97 cases differ. They were variously diagnosed as hypermenorrhea, chronic bilateral oophoritis with cystic ovaries and fibroma of uterus with cystic ovaries.

Twenty-two patients, whose ages varied from 21 years to 40 years, presented the following type of picture. The average catamenic history for this group is: menses, established at 13 years, recur every 40 days and last only 2 days. Gross examination reveals uteri that are smaller than normal, salpinges that are hypoplastic, ovaries that are hyperinterstitial and hypofollicular. Pathologic examination shows an ovarian cortex with an increase of fibrous tissue. There is a hyperinterstitial ovarian matrix. There is a cystic degeneration of occasional follicles. Arteries show an endarteritis. There is a plexus of dilated vessels in the hilus.

Summary

Follicle maturation is inhibited in ovaries that are hyperinterstitial. Consequently, there is an estrone deficiency and therefore, a hypoplasia of salpinges, uterine body, endometrium and vaginal mucosa.

Follicle maturation is uninhibited in hypointerstitial ovaries. Consequently, there is an estrone overabundance and therefore, a hyperplasia of the salpinges, uterine body, endometrium and vaginal mucosa.

Conclusions

Hyperinterstitial ovaries elaborate an insufficient quantity of estrone.

Hypointerstitial ovaries elaborate an excessive quantity of estrone.

269 S. 19th Street.

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LUDWIG'S ANGINA

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Historical

LUDWIG'S angina has been discussed by many authors during the past one hundred years. A brief reference to the literature discloses that these writers are far from unanimous in their opinions as to its causes and equally divergent in their discussions of the clinical picture. The disease was first described by Ludwig of Stuttgart in 1836[1] as an acute inflammatory process beginning in the submaxillary region where it soon assumes a character which he termed "gangrenous inflammation of the neck."

Lederer[2] described the disease as a virulent, extensive, phlegmonous process arising from infections within the floor of the mouth and localized to a definite anatomic space in the sub-mandibular region. Barnhill[3] stated that Ludwig's angina is characterized by infiltration of the tissues of the floor of the mouth and neck below the border of the inferior maxilla. On the other hand, McKenzie[4] considered the disease a form of septic cellulitis or erysipelas of the submaxillary region. It is generally agreed that bacteriologically we are dealing most commonly with a pure streptococcic infection although staphylococcus, diplococcus, pneumococcus, bacillus septicus, Vincent's organisms and Friedlander's bacillus have been held responsible by various investigators.

In discussing the etiology it is again apparent that the reports differ extensively. According to Lederer, infection originates in a carious tooth, tonsillitis or mouth ulcer and passes from inside the mouth to the submaxillary region by following the fascial plane of the mylohyoid muscle. However, while agreeing with Lederer that infection may occur within gingival borders, Jackson and Coates[5] pointed out that experimental studies of the lymphatic drainage have established that such infections can not come from the region of the faucial tonsils. McKenzie believed that Ludwig's angina is secondary to a streptococcic or pneumococcic glossitis or pharyngitis, while Morrison[6] placed the origin of infection in the floor of the mouth, spreading, late in its course, down all the fascial planes as a phlegmon into one or both submaxillary areas involving the entire neck on one or both sides. This latter condition then gives rise to laryngeal edema with possible asphyxia, jugular vein thrombosis and pyemia or mediastinitis if left untreated.

The clinical picture, as reported by Lederer, is characterized by severe involvement of the cervical cellular tissue and profound tox-

emia. The rapidly spreading cellulitis, because of anatomic relationships, invades the larynx, trachea and lungs with general systemic infection and frequently with fatal results. Blassingame[7] and Morrison found an infection with abscess formation or diffuse cellulitis producing a hard, tender swelling in the floor of the mouth, pushing the tongue up to the roof of the mouth and making its motion extremely difficult and painful. They found no actual trismus, but the tongue prevented the mouth from being opened widely. In contrast with this McKenzie described Ludwig's angina as characterized by the formation of a hard, brawny swelling of the parts under the jaw and in the upper cervical region. General phlegmonous swelling of the floor of the mouth, the fauces, the pharynx and larynx coexisted with severe constitutional disturbances. Multiple abscesses of the neck were observed in patients surviving the early stage. There is a grave danger to life from septicemia, edema of the glottis with early asphyxiation or later from exhaustion.

With this resume of the similarities and differences in the conclusions reached by earlier investigators, let us proceed to a new approach to the diagnosis and treatment of Ludwig's angina as demonstrated in the reports of two cases.

Diagnosis and Treatment

The treatment of Ludwig's angina should be based upon careful consideration and study of the anatomy of the mouth and base of the jaw. It seems regrettable that a tentative diagnosis of Ludwig's angina often causes consternation to the attending surgeon. Because of the known high mortality of this condition and the infrequency of its occurrence there is a tendency to proceed immediately with a so-called classical incision which, by a careful study of the patient, would clearly be shown to be irrational. In approaching the subject let us first consider briefly the anatomy of the neck in so far as it is pertinent to such a discussion (fig. 1).

In the portion of the neck referred to above, the platysma myoides lies directly under the skin. Next is found the digastric muscle, consisting of anterior and posterior bellies. Above it, is the mylohyoid with its diagonal fibers meeting in a median line. Above that, lies the geniohyoid on which the geniohyoglossus rests. Above and on either side of the geniohyoid, lie the lingual muscles and the tongue musculature. All of these muscles originate in some part of the mandible anteriorly and, with the exception of the lingual muscle, insert themselves in the hyoid bone. The stylohoid muscle, running from the hyoid to the styloid process, elevates the hyoid bone on deglutition. A small portion of the posterior border

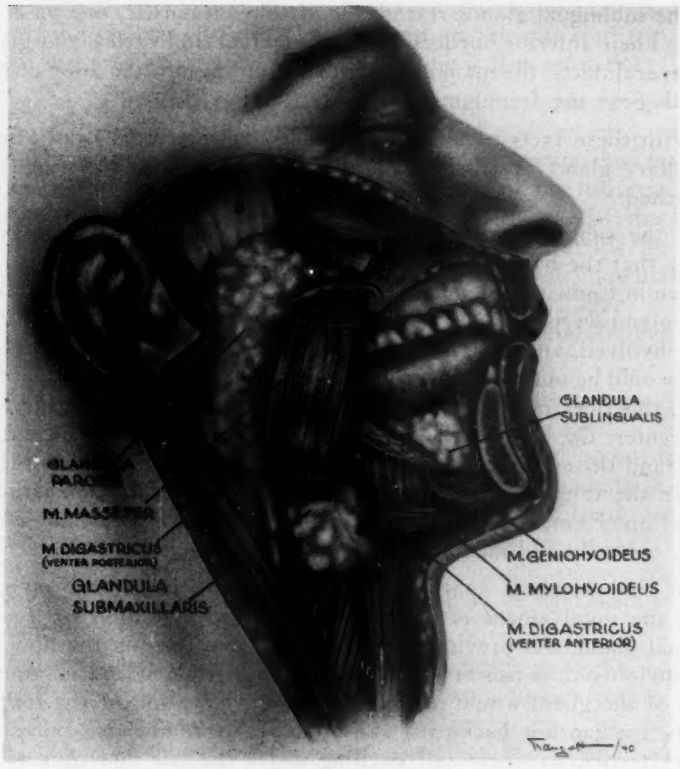

Fig. 1. The anatomic structures concerned in Ludwig's angina.

of the mylohyoid muscle is free from any bony attachment. The submaxillary gland is partially supported by it.

The submaxillary gland is situated below the horizontal ramus of the mandible near its angle. It occupies a space bounded externally and above by the inner surface of the mandible, externally and below by the skin and fascia, and internally by the myohyoid muscle. The posterior and greater portion of the gland also rests internally on the hyoglossus, the posterior belly of the digastric and the stylohyoid muscles. This portion very often reaches to the anterior border of the sternocleidomastoid muscle. Thus it should be noted that the submaxillary gland is more external and (with the exception of its Wharton's duct) is separated from the floor of the mouth by musculature. It is most readily palpable externally and laterally, beneath the angle of the jaw and, as is clearly shown in fig. 1, is far removed from the similar gland on the opposite side.

The sublingual glands rest on the mylohyoid muscle, one on each side. Their anterior borders lie close together and each gland gives off several ducts, the main one of which empties into the floor of the mouth near the frenulum.

With these facts of anatomy in mind, consideration of the submaxillary gland as a principal causative factor may be better approached.

If the submaxillary gland were involved initially it seems unlikely that the base of the tongue would be pushed up medially as is seen in Ludwig's angina. One would believe that if the submaxillary gland were involved the tongue would be elevated first on the side involved, and that the greater amount of swelling and tenderness would be outward laterally toward the angle of the jaw. However, this does not appear to be the case. The elevation begins in the center, the base of the tongue is pushed back evenly on either side, and the swelling and hardness appear more medially, directly under the tongue. Also, it seems doubtful that the submaxillary gland involvement would produce a hard, boil-like mass under the chin, centrally and medially.

In view of these anatomic considerations I am of the opinion that the involvement is strictly an abscessed condition of a sublingual gland. As previously stated, this gland lies on the floor of the mylohyoid, is close to the other sublingual gland and inflammation of the gland would immediately cause elevation of the tongue in the median line backward and upward. It would also cause the characteristic hardness and swelling under the jaw and chin which produce difficulty in swallowing as well as in breathing by reason of the upward pressure of the tongue. This depresses the epiglottis and the downward pressure in turn forces the hyoid bone downward and outward.

In my opinion any inflammatory process in the region of the sublingual gland which produces the classical symptoms attributed to the disease can be classified as Ludwig's angina. Thus it is not a disease per se but may be classed as a clinical entity only because of the location of the abscess. When pus is located, one cannot differentiate between this abscess inflammation and that of any other glandular abscess since bacterial findings indicate only the causative organisms and are, therefore, inconclusive.

Since the sublingual gland lies on the mylohyoid muscle and can be reached most easily through the oral region, and since any opening made externally merely tends to injure the musculature and the support which is given to these glands, it seems most rational to attack this involvement intra-orally. Such attack must be made

in its early stages. My method of treatment includes first the support of the area involved by means of rest and elevation of the part (just exactly as we support an involved limb if it is infected).

Bearing in mind that the base of the tongue is pressed upward and that the hyoid bone is pressed downward and outward, relief of the distressing respiratory difficulties may be accomplished by the application of adhesive tape to exert force upward and inward. The tape is applied from one side of the jaw at the base of the ear, around the throat and up the opposite side. Several strips are applied partially overlapping each other. By this means musculature and hyoid bone are somewhat raised and a better air space is created in the throat since we have no method of successfully depressing the elevated base of the tongue.

Once adequate support is established, the next step is to expose the area of infection underneath the tongue by making an incision along the floor of the mouth, exposing the sublingual gland itself. The gland is then incised and the areolar tissue surrounding it is loosened. After this, blunt hemostatic forceps are employed to spread the area of incision providing for adequate drainage. It might be said parenthetically that prior to incision, puncturing of the area by means of an aspirating needle may be of assistance in locating the exact site of involvement.

The next step is to provide for adequate drainage of the wound without unnecessary trauma and with minimum discomfort to the patient. To my mind, the insertion of drains whether of rubber, tissue, gauze or tubing is unnecessary provided the wound is kept irrigated to permit free drainage. In addition to the surgical measures and the support described above, the use of sulfanilamide is indicated if streptococcus is found to be the predominating organism. However, keeping the wound open for frequent irrigation and cleansing is most important and any agents used in this respect must be mild, non-irritating and bactericidal.

The necessity for choice of a suitable solution brought to mind a previous experience in a case of acute suppurative inflammation of the deep tissues of the neck which had been described (by me) in an earlier paper[8], in which a Council Accepted solution of azochloramid[9] had been employed with satisfactory results. In addition, the literature[10, 11, 12] indicated the unusual blandness, prolonged efficacy and non-toxicity of this chlorine preparation.

For irrigation I employed the aqueous solution of azochloramid 1:3300 which is isotonic, buffered to *p*H 7.4 and contains no alkali. I feel that the use of this solution contributed materially to the successful outcome of the following cases:

Report of Cases

Case 1.—On April 6, 1939, a male patient, B. B., a 19 year old student, experienced a feeling of fulness in the throat which persisted for 48 hours. He then began to have pain on swallowing which increased until he was compelled to seek medical attention. He was seen by me on April 13, when examination revealed a marked edema under the tongue on both sides, and an ele-

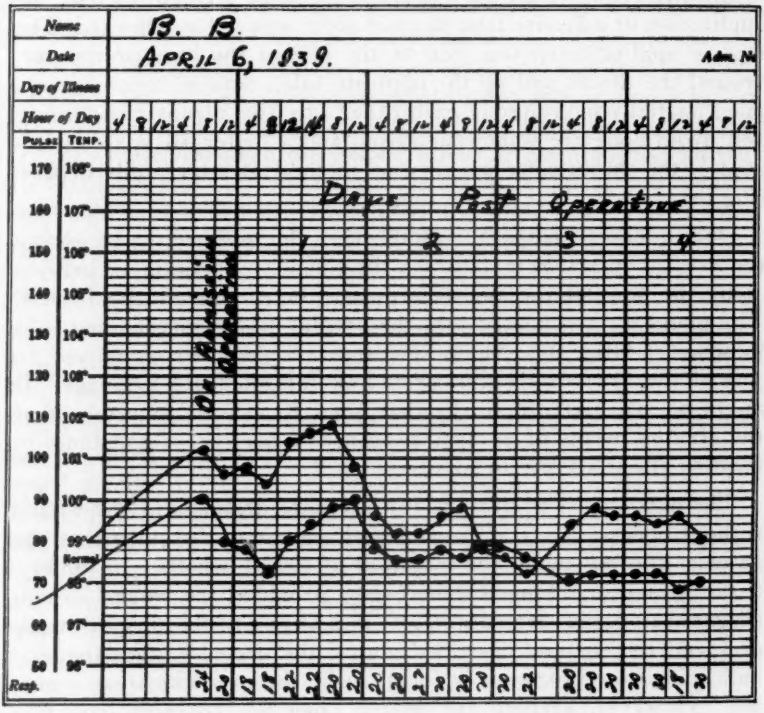

Fig. 2. The temperature, pulse and respiration in Case 1.

vated and upward protruding tongue which interfered with articulation and deglutition. There was a hard, immovable, brawny mass in the sublingual area which was palpable externally. Temperature at this time was 101.2°, pulse 100. The patient was taken immediately to the hospital where a four inch needle was inserted in three different places in the sublingual area on both sides of the tongue. At the third insertion, pus was encountered on the left side yielding about one drachm. Under topical anesthesia, an incision was made under the left side of the tongue where the pus was found. With hemostatic forceps, tissue in this area was separated and more pus released. A metal suction tip attached to a suction machine was inserted in the open wound for the purpose of removing some blood and purulent matter. The wound was then irrigated with a 1:3300 warm solution of azochloramid.

On culture the pus was positive for hemolytic streptococcus, which predominated, and for Staphylococcus albus. Having in mind the difficulty of main-

taining a rubber drain in this area, I decided to apply intraoral irrigation and suction. Irrigation with azochloramid saline solution 1:3300 was carried on every two hours for the first day and night without interruption. As supportive measures the lower jaw was taped with adhesive from ear to ear, an ice collar was applied to the neck and 10 c.c. of prontosil was injected by vein every four hours.

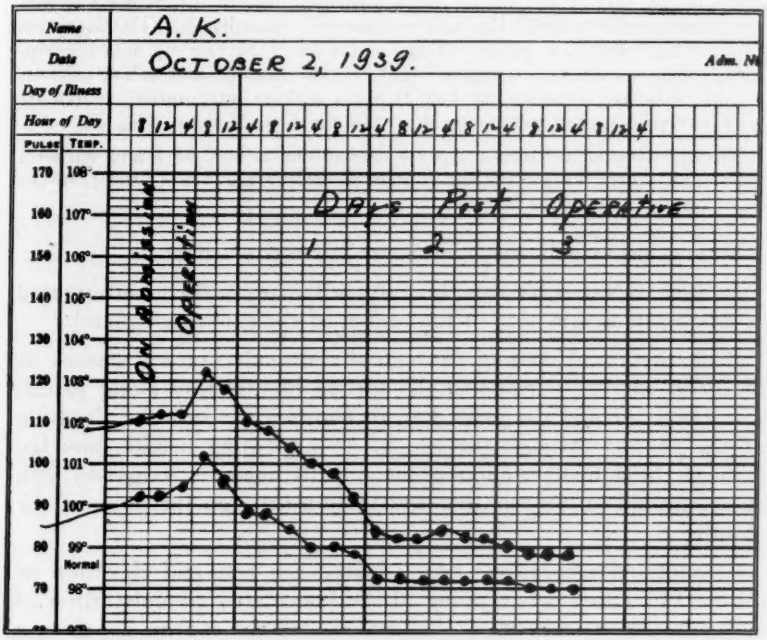

Fig. 3. The temperature and pulse in Case 2.

On the second day the patient was allowed to rest at night without being disturbed for irrigations. The temperature, which had risen to 101.8° after operation, dropped gradually to 99.2° on the day following surgical intervention (fig. 2). Irrigations with azochloramid saline solution 1:3300 were continued and, as the patient was able to take liquids more freely than previously, ten grains of sulfanilamide were given orally every four hours instead of the prontosil injections.

It may be of interest to note that on the second postoperative day the patient was able to take nourishment with relatively little inconvenience or pain. For a period of one week the wound was kept open to prevent closure while pus was still forming. Subsequently the lesion closed uneventfully. On April 22 the patient was discharged from the hospital.

Case 2.—On Oct. 1, 1939, Mr. A. K., aged 29, felt a swelling underneath his tongue accompanied by severe pain while eating. Slight relief was afforded only upon elevating his tongue toward the roof of his mouth. The patient was seen by me on October 2 at which time there was visible swelling beneath

the tongue, more marked on the right side. The tongue was elevated, interfering with articulation and deglutition, with an immovable, hard, brawny mass in the sublingual area, palpable internally as well as externally. The temperature was 102°, pulse 92.

The patient was immediately prepared for operation. Under topical anesthesia, using 4 per cent cocaine hydrochloride solution applied by pledgets of cotton on the floor of the mouth, an incision was made in the right sublingual area, beneath the tongue. Pus was encountered immediately. The area was explored for additional pockets of pus and a metal suction tip was then inserted. The wound was irrigated with warm azochloramid saline solution 1:3300 every two hours for the first 24 hours without interruption, as in Case 1. There was marked improvement within the first 24 hours (fig. 3).

The same supportive measures were carried out as in Case 1 and within a short time thereafter the patient completely recovered. On October 10, he was discharged from the hospital.

In conclusion it is the opinion of this writer that:

1. Ludwig's angina may be rationally approached and treated as an abscess originating in the region of the sublingual gland.

2. Rather than incising through the musculature and tissues of the neck, thereby permitting the spread of infection along fascial and muscle planes, the procedure of choice appears to be: location of the abscess through the use of an aspirating needle, inserted through the floor of the mouth intra-orally, incision, irrigation with azochloramid saline solution, and suction through the floor of the mouth.

3. Supportive measures best adapted are rest and elevation of the part by adhesive strapping of the lower jaw, administration of sulfanilamide if streptococci are found, and the routine use at first of prontosil injections, followed by sulfanilamide taken orally when the patient is able to swallow.

2600 Boulevard.

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THE RICHMOND ASSEMBLY

While it took the Yankees four years to capture the Capital of the Confederacy, it took The Southeastern Surgical Congress twelve to get into the city but when it did, the Congress surrendered completely to the charms of Richmond. The grand old city was so delightful that it was rather difficult to keep the pilgrims in the auditorium. We should warn our recent hosts that they should never invite us back again unless they really want us. Those who failed to get to Williamsburg this time are just looking for an excuse to get back to Virginia.

It may be only because the meeting is so fresh in our minds, but it would seem that the Program was the best yet. Dr. Abell's Presidential Address is the first paper in this issue of the SURGEON. The C. Jeff Miller Lecture was delivered by the President of the American Medical Association, Dr. Frank H. Lahey. Dr. Brien T. King described his operation for restoring speech in cases of bilateral abductor cord paralysis: A lady who had been unable to talk for four years before Dr. King operated on her in Seattle, happened to be in Washington, D. C. at the time of the meeting and she graciously consented to appear before the Congress to prove that her voice was perfect.

It would be supererogatory to mention any other papers, for the reader will be able to judge for himself when they appear in these pages. A trend toward conservatism in surgery was noted, even when brand new operative procedures were described. The discussions of traumatic surgery were particularly timely. One must also remark on the splendid presentations made by the younger Fellows of the Congress.

FELLOWS OF THE SOUTHEASTERN SURGICAL CONGRESS MEET

At the business meeting of the Fellows reports were received from the component States. These showed a healthy growth of the Congress, particularly in Tennessee, Virginia and Alabama.

The following deaths were announced:

DR. CECIL D. GASTON
Birmingham
Sept. 12, 1940

DR. W. W. HARPER
Selma, Alabama
Jan. 14, 1941

DR. RALPH E. STEVENS
Chattahoochee, Florida
June 6, 1940

DR. S. D. GAUSEMEL
Atlanta
Jan. 17, 1941

DR. W. M. SCOTT
Milledgeville, Georgia
Oct. 31, 1940

DR. JOHN G. MARTIN
Lake Charles, Louisiana

A certified financial statement of the Congress was read by the Secretary-Treasurer. This showed that, after publishing THE SOUTHERN SURGEON monthly for a year, the state of the exchequer was better than ever.

A motion was carried that those Fellows called into active military service, who requested the remission of their dues, be exempted from paying them until after they had returned to private practice.

The following telegram was sent to the President:

"The Southeastern Surgical Congress, whose membership includes more than six hundred of the leading surgeons in eleven of the Southeastern States, in session in Richmond, Virginia, at this time, desires to offer through you its services to our country in this grave world crisis:

"1. To protect the health of the rank and file of the citizens of this country.

"2. Zealously to guard health standards among the industrial and farm populations engaged in the production of supplies for ourselves and our democratic neighbors to the end that the preparedness program may not be handicapped nor progress impeded, and

"3. In case of hostilities, against which we know that you have striven and will strive with all the force of your inspired leadership, to place its services at the disposal of the Government to the end that the lives and health of

our comrades may be more effectively safeguarded and pain and suffering minimized."

A few hours later the following reply was read:

"Please accept the President's thanks for your splendid telegram of March eleventh pledging the services of The Southeastern Surgical Congress in promoting the National Defense by protecting the health of the nation, particularly in guarding health standards among industrial and farm populations engaged in the production of defense material. This voluntary pledge of loyal support is most reassuring to the President in the grave responsibilities before him.

"STEPHEN EARLY, Secretary to the President."

Dr. Alton Ochsner, of New Orleans, was made President-Elect and, in recognition of his services as General Chairman of the Richmond meeting, Dr. Frank S. Johns was elected Vice President. Dr. Julian L. Rawls, of Norfolk, having been elected in 1940, was elevated to the Presidency.

Although several cordial invitations for the 1942 Assembly were received, in view of unsettled conditions the selection of the place for the meeting next year was deferred.